

86. A compound according to claim 65 wherein two adjacent groups of an aromatic ring in the substituted C1-C6-alkoxy may form an additional ring over a methylenedioxy bridge.

REMARKS

Applicant's attorneys thank the Examiner for the Interview on March 13, 2002. Upon entry of the present amendment, claims 42-46, 56, 64, 65-71, 77, and 82 have been amended, claims 83-86 have been added, and claims 42-51 and 55-86 are pending. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made".

Applicant responds to the paragraphs in the last office action as follows.

Paragraph 1: 35 USC 112, 2nd Paragraph Rejections

"C₁-C₆-alkoxycarbonyl" has been changed to "C₂-C₆-alkoxycarbonyl".

Paragraph 2: Rejection of claims 42-46, 56-58, 62, 68 and 70 under 35 USC 103(a) over EP 0330026

Provided herewith is a declaration described and requested at the first interview. Also we have deleted "additional active ingredient" in claims as per the request at the last interview. See claim 66.

The '026 reference describes compounds for the treatment of Alzheimer's disease. The '026 reference describes a 1,3 pyridine compound at page 12 of the ref, see compound 13. It does not describe or suggest the importance of compounds that include a pyridine ring,

substitution in the 3 position (see declaration re compounds 312 vs 312A2 also see 159A2),

the criticality of "A" (see declaration compound 312 vs 159.C),

or the importance of having an amide group in the chain of the substituent attached to the 3 position as claimed (see 312 vs 312.D1 and 312.D2). The importance of these selections and positions is described in the attached Declaration.

The '026 reference describes unsaturated carboxylic acid amide derivatives. One of ordinary skill reading the '026 reference would not have been taught the criticality of making certain substitution and selecting the combination as claimed. Hence, in the art would have no motivation to make compounds as now claimed.

Paragraphs 3 and 4: Obviousness type double patenting

Applicants will provide a terminal disclaimer upon notice of allowability.

As request by the Examiner at the last interview, the following pending applications that have related subject matter. Serial Nos. 09/216,075, 09/216,482, 09/596,001, 09/595,547, 09/595,218, 09/596,086, and 09/935,772.

Paragraph 5: 35 USC 112, 2nd Paragraph Rejections

Claim 64 amended to indicate "administering to the human or animal body in need thereof an amount of pharmaceutical composition effective for inhibiting tumor cell growth".

Claim 65 amended to indicate "administering to the human or animal body in need thereof an amount of pharmaceutical composition effective for suppressing autoimmune disease".

Claim 66 amended to indicate "administering to the human or animal body in need thereof an amount of pharmaceutical composition effective for inhibiting tumor cell growth".

Claim 67 amended to indicate "administering to the human or animal body in need thereof an amount of pharmaceutical composition. effective for suppressing autoimmune disease".

Paragraph 6: Rejection of claims 45-46 under 35 USC 103(a)
over EP 0330026

See paragraph 2

Paragraph 7: Publication Date on IDS

The publication date of the reference is January 1999.

Paragraph 8: Improper Markush Group

Election was made where E is piperidine. All pending claims require E to be a piperidine.

Paragraph 9: Correction of Variables in claims 70 and 71

The variables in claims 70 and 71 have been amended to make them consistent with those set forth in claim 42.

Paragraph 10: Support for Pharmaceutically Acceptable Salts

Claims have been amended to indicate "pharmaceutically acceptable acid addition salts" (see page 128 and 131 of the specification).

Paragraph 11: Support for "D"

Claims 69 and 70 have been amended to make the definition of "D" consistent with claim 42.

Paragraphs 12-18: Support for Structures

Structures have been deleted which do not have proper antecedant basis.

Paragraph 19:

a) Claims 42, 56, 64, 65 and 69 have been amended to change "(CH=CH)-" to "-(CH=CH)-". Support for this amendment is at page 4, line 16 of the specification.

b) Claims 42, 43, 56, 64, 65 and 69 have been amended to change "Ar₂" to "Ar²".

c) Claims 42, 43, 56, 64, 65 and 69 have been amended to change "Ar₂" to "Ar²".

d) Claims 42, 43, 44, 56 and 65 have been amended to delete "wherein two adjacent groups of an aromatic ring in the substituted C1-C6 alkoxy may form an additional ring". This limitation has been added in dependent claims 83-86.

e) In Claim 43 "isosterically replaced C1 to C8 group" has been rewritten as discussed.

f) In Claim 43 "bound directly over a methylene group, furyl, thienyl, pyrrolyl, oxazolyl . . ." has been deleted and/or rewritten as discussed.

g) In Claim 44 "isosterically replaced C2 to C8 group" has been rewritten as discussed.

h) The word "and" has been deleted from the definition of R¹² in claim 44.

i) In Claim 44 "bound directly or over a methylene group . . ." has been rewritten as discussed.

j) In Claim 44 and 45, antecedant basis for "-NR¹²R¹⁴" in claim 42 has been provided as discussed.

k) In claims 44 "indol" has been changed to "--inodole--".

l) Claim 45 has been amended to be dependent on claim 44.

m) Claim 45 has been amended to clarify that the double bond of the C₂-C₆ alkenylene may be to ring E.

n) In Claim 45 "an isosterically replaced C2 to C6 group." has been rewritten as discussed.

o) In Claim 45 "bound directly or over a methylene group . . ." has been rewritten as discussed.

p) Claim 46 has been amended to clarify that the double bond of the C₂-C₆ alkenylene may be to ring E.

r) Claim 68 has been amended to delete the second occurrence of "hydrogen".

s) The word "and" has been deleted from the definition of R¹² in claim 68.

t) Claim 69 has been amended to delete the second occurrence of "selected from" from the definition of R⁹.

u) In Claim 60 "N, S, and O being bound directly to or over a methylene group" has been rewritten as discussed.

v) Claim 70 has been amended to delete "C₄-C₆ alkenylene".

w) Claim 70 has been amended to delete the second occurrence of "selected from" from the definition of R⁹.

x) Claim 70 has been amended to change "R" to "R¹⁴".

y) Claim 70 has been amended to delete the second occurrence of "C₃-C₆ alkenyl" in the definition of R⁴ (now R¹²).

z) Claim 71 has been amended to delete the second moiety on page 80 of the amendment filed on 9/5/01.

aa) Claim 71 has been amended to delete the moiety on page 81 of the amendment filed on 9/5/01.

ab) Claim 71 has been amended to delete the fourth moiety on page 88 of the amendment filed on 9/5/01.

ac) Claim 77 has been amended to delete the second moiety on page 116 of the amendment filed on 9/5/01.

ad) Claim 77 has been amended to delete the moiety on page 117 of the amendment filed on 9/5/01.

ae) Claim 77 has been amended to delete the fourth moiety on page 88 of the amendment filed on 9/5/01.

af) Claim 82 has been amended to delete the second moiety on page 151 of the amendment filed on 9/5/01.

ag) Claim 82 has been amended to delete the moiety on page 152 of the amendment filed on 9/5/01.

ah) Claim 82 has been amended to delete the fourth moiety on page 159 of the amendment filed on 9/5/01.

Applicants respectfully request that in view of the amendments and remarks made herein that the pending claims be passed to issue.

Respectfully submitted,

FITCH, EVEN, TABIN & FLANNERY

By 

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Date:

APR 10 2002

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PATENT
ATTORNEY DOCKET
NO. 64978

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Biedermann et al.)
Serial No.: 09/242,540)
Filed: February 18, 1999)
Title: PYRIDYL ALKENE AND)
PYRIDYL ALKINE-ACID)
AMIDES AS CYTOSTATICS AND)
IMMUNOSUPPRESSIVES)
Group Art Unit: 1624)
Examiner: B. Coleman)

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AMENDMENT B - Version with Brackets and Underlining

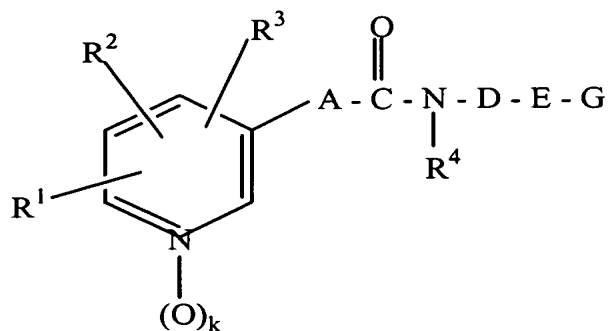
Honorable Commissioner of Patents
and Trademarks
ATTENTION: Assistant Commissioner
for Patents
Washington, D.C. 20231

Dear Sir:

In response to the office action dated November 15, 2001,
please amend the above-identified application as follows.

IN THE CLAIMS:

42. (twice amended) A compound of formula (I) and
pharmaceutically acceptable acid addition salts of formula (I)



(I)

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wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_4 -hydroxyalkyl, hydroxy, C_1 - C_4 -alkoxy, benzyloxy, C_2 - C_4 -alkanoyloxy, C_1 - C_4 -alkylthio, C_2 - C_5 -alkoxycarbonyl, aminocarbonyl, C_3 - C_9 -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR^5R^6 , and bridged R^1R^2 wherein

R^5 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl; and

R^6 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl;

R^2 is selected from the group consisting of hydrogen, halogen, C_1 - C_6 -alkyl, trifluoromethyl and hydroxy and bridged R^1R^2 ;

wherein

bridged R^1R^2 is where R^1R^2 are adjacent and form a bridge which is selected from the group consisting of $-(CH_2)_4-$, $-(CH=CH)_2-$ and $-CH_2O-CR^7R^8-O-$; wherein

R^7 is selected from the group consisting of hydrogen, and

C₁-C₆-alkyl; and

R⁸ is selected from the group consisting of hydrogen and C₁-C₆-alkyl;

R³ is selected from the group consisting of hydrogen, halogen and C₁-C₆-alkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, cyano, or phenyl, C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, or cyano, and ethynylene;

D is selected from the group consisting of C₁-C₁₀-alkylene,

a substituted C₁-C₁₀-alkylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

C₂-C₁₀-alkenylene,

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

a C₂-C₁₀-alkenylene wherein the double bond is to ring E,

a substituted C₂-C₁₀-alkenylene which is substituted once

or twice by C_1 - C_3 -alkyl or hydroxy, wherein the double bond is to E,

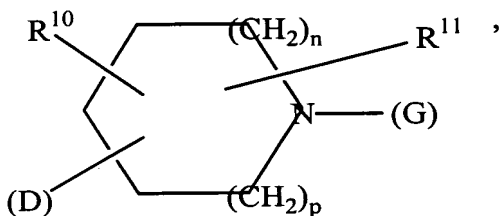
C_3 - C_{10} -alkynylene,

a substituted C_3 - C_{10} -alkynylene which is substituted once or twice by C_1 - C_3 -alkyl or hydroxy,

[an isosterically replaced] a C_1 to C_{10} group selected from the group consisting of C_1 - C_{10} -alkylene, C_2 - C_{10} -alkenylene and C_3 - C_{10} -alkynylene, the [isosterically replaced] C_1 to C_{10} group having methylene units [and] wherein one to three of the methylene units are isosterically replaced by O, S, NR^9 , CO, SO or SO_2 ; wherein

R^9 is selected from the group consisting of hydrogen, C_1 - C_3 -alkyl, C_2 - C_6 -acyl and methanesulfonyl;

E is



wherein n and p are, independent of each other, 0, 1, 2, or 3, wherein $n + p \leq 3$,

R^{10} is selected from the group consisting of hydrogen, C_1 - C_3 -alkyl, hydroxy, hydroxymethyl, carboxy and C_2 - C_7 -alkoxycarbonyl;

R^{11} is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen, G1, G2, G3, G4 and G5; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$
wherein

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from the group consisting of hydrogen,

C_1 - C_6 -alkyl,

C_3 - C_6 -alkenyl,

C_3 - C_6 -alkinyl,

C_3 - C_8 -cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered heterocycles which heterocycles contain one to three hetero-atoms selected from the group consisting of N, S and O, which heterocycles are either bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

an [N, S, O] anellated bi- and tricyclic aromatic or



43

partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from N, S and O and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group;

R^{13} has the same meaning as R^{12} , but is selected independently thereof,

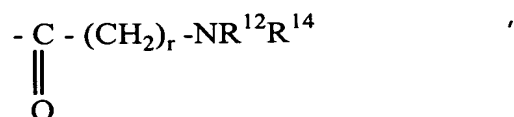
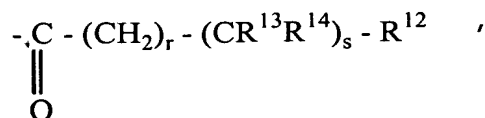
R^{14} is selected from the group consisting of hydrogen,
hydroxy,
methyl,
benzyl,
phenyl,

monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

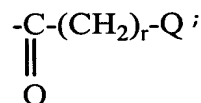
an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

an [N, S, O] anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms [are] selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group;

G2 is selected from the group consisting of



and



wherein R^{12} and R^{14} have the above meaning, and Q is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

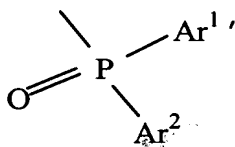
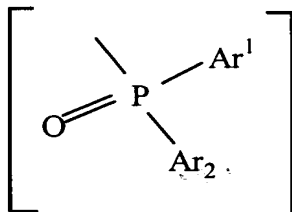
saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, and

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

G3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{12}$,

G4 is



wherein

Ar^1 is selected from the group consisting of phenyl, pyridyl and naphthyl; and

Ar^2 is selected from the group consisting of phenyl, pyridyl and naphthyl;

G5 is $-\text{COR}^{15}$,

wherein

R^{15} is selected from the group consisting of trifluoromethyl, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy and benzyloxy; and

wherein aromatic rings in R^1 , R^4 , R^{12} , R^{13} , R^{14} , R^{15} , Q, Ar^1

and Ar^2 are unsubstituted or substituted, the substituted rings in R^1 , R^4 , R^{12} , R^{13} , R^{14} , R^{15} , Q , Ar^1 and Ar^2 having one to three substituents which are independently selected from the group consisting of halogen, cyano, $\text{C}_1\text{-C}_6\text{-alkyl}$, trifluoromethyl, $\text{C}_3\text{-C}_8\text{-cycloalkyl}$, phenyl, benzyl, hydroxy, $\text{C}_1\text{-C}_6\text{-alkoxy}$, and a substituted $\text{C}_1\text{-C}_6\text{-alkoxy}$ which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, $\text{C}_1\text{-C}_6\text{-alkylthio}$, carboxy, $[\text{C}_1]\text{C}_2\text{-C}_6\text{-alkoxycarbonyl}$, benzyloxycarbonyl, nitro, amino, mono- $\text{C}_1\text{-C}_6\text{-alkylamino}$, and di- $(\text{C}_1\text{-C}_6\text{-alkyl})\text{-amino}$, [wherein two adjacent groups of an aromatic ring in the substituted $\text{C}_1\text{-C}_6\text{-alkoxy}$ may form an additional ring over a methylenedioxy bridge,] wherein general formula (I) does not include (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-2-propenamide.

43. (Twice amended) A compound according to claim 42, wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, methyl, trifluoromethyl, hydroxy, $\text{C}_1\text{-C}_4\text{-alkoxy}$, ethylthio, methoxycarbonyl, tert-butoxycarbonyl, aminocarbonyl, carboxy, and phenoxy,

R^2 is selected from the group consisting of hydrogen, halogen, trifluoromethyl and hydroxy,

R^3 is hydrogen or halogen,

R^4 is selected from the group consisting of hydrogen, $\text{C}_1\text{-C}_3\text{-alkyl}$, hydroxy and $\text{C}_1\text{-C}_3\text{-alkoxy}$,

k is 0 or 1,



44

A is selected from the group consisting of C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once or twice by C₁-C₃-alkyl, hydroxy or fluorine,

a C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted by C₁-C₃-alkyl or by 1 or 2 fluorine atoms,

1,3,5-hexatrienylene, and

a substituted 1,3,5-hexatrienylene which is substituted by fluorine,

D is selected from the group consisting of C₁-C₈-alkylene,

a substituted C₁-C₈-alkylene which is substituted once or twice by methyl or hydroxy,

C₂-C₈-alkenylene,

a substituted C₂-C₈-alkenylene which is substituted once or twice by methyl or hydroxy,

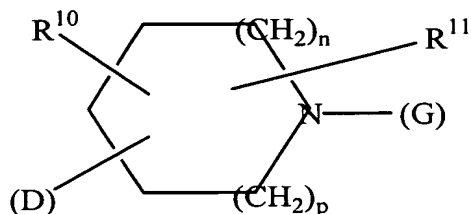
an E double bonded substituted C₂-C₈-alkenylene which has a double bond to ring E,

C₃-C₈-alkynylene,

a substituted C₃-C₈-alkynylene which is substituted once or twice by methyl or hydroxy, and

[an isosterically replaced] a C₁ to C₈ group selected from the group consisting of C₁-C₈-alkylene, C₂-C₈-alkenylene and C₃-C₈-alkynylene, the [isosterically replaced] C₁ to C₈ group having methylene units [and] wherein one to three methylene units are isosterically replaced by O, S, NH, N(CH₃), N(COCH₃), N(SO₂CH₃), CO, SO or SO₂,

E is



wherein n and p are, independent of each other, 0, 1, 2, or 3, wherein $n + p \leq 3$,

R^{10} is selected from the group consisting of hydrogen, C_1 - C_3 -alkyl, hydroxy, hydroxymethyl, carboxy and C_2 - C_7 -alkoxycarbonyl;

R^{11} is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen, G_1 , G_2 , G_3 , G_4 and G_5 ; wherein

G_1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$
wherein

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_8 -cycloalkyl, benzyl, phenyl, benzocyclobutyl, indanyl, indenyl, oxoindanyl, naphthyl, dihydronaphthyl, tetrahydronaphthyl, oxotetrahydronaphthyl, biphenylenyl, fluorenyl, oxofluorenyl, anthryl, dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl, phenanthryl,

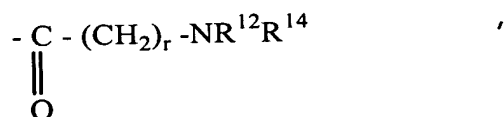
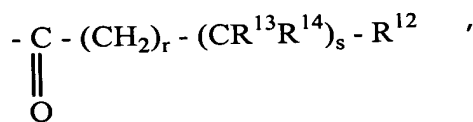
dihydrophenanthryl, oxodihydrophenanthryl,
dibenzocycloheptenyl, oxodibenzocycloheptenyl,
dihydrodibenzocycloheptenyl, oxodihydrodibenzocycloheptenyl,
dihydrodibenzocyclooctenyl, tetrahydrodibenzocyclooctenyl and
oxotetrahydrodibenzocyclooctenyl, [bound directly or over a
methylene group,] furyl, thienyl, pyrrolyl, oxazolyl,
isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl,
oxadiazolyl, thiadiazolyl, triazolyl, pyridyl, pyrazinyl,
pyridazinyl, pyrimidinyl, triazinyl, imidazothiazolyl,
benzofuryl, dihydrobenzofuryl, benzothienyl,
dihydrobenzothienyl, indolyl, indolinyl, oxoindolinyl,
dioxoindolinyl, benzoxazolyl, oxobenzoxazolyl,
benzisoazolyl, oxobenzisoazolyl, benzothiazolyl,
oxobenzthiazolyl, benzoisothiazolyl, oxobenzoisothiazolyl,
benzimidazolyl, oxobenzimidazolyl, indazolyl,
oxoindazolyl, benzofurazanyl, benzothiadiaazolyl,
benzotriazolyl, oxazolopyridyl, oxodihydrooxazolopyridyl,
thiazolopyridyl, oxodihydrothiazolopyridyl,
isothiazolopyridyl, imidazopyridyl, oxodihydroimidazopyridyl,
pyrazolopyridyl, oxodihydropyrazolopyridyl, thienopyrimidinyl,
chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl,
isoquinolyl, dihydroquinolyl, oxodihydroquinolyl,
tetrahydroquinolyl, oxotetrahydroquinolyl, benzodioxanyl,
quinoxalyl, quinazolyl, naphthyridyl, carbazolyl,
tetrahydrocarbazolyl, oxotetrahydrocarbazolyl, pyridoindolyl,
acridyl, oxodihydroacridyl, phenothiazyl,
dihydrodibenzoxepinyl, oxodihydrodibenzoxepinyl,
benzocycloheptathienyl, oxobenzocycloheptathienyl,
dihydrothienobenzothiepinyl, oxodihydrothienobenzothiepinyl,
dihydrodibenzothiepinyl, oxodihydrodibenzothiepinyl,
octahydrodibenzothiepinyl, dihydrodibenzazepinyl,
oxodihydrodibenzazepinyl, octahydrodibenzazepinyl,

benzocycloheptapyridyl, oxobenzocycloheptapyridyl, dihydropyridobenzodiazepinyl, dihydrodibenzoxazepinyl, dihydropyridobenzoxepinyl, dihydropyridobenzoxazepinyl, oxodihydropyridobenzoxazepinyl, dihydrodibenzothiazepinyl, oxodihydrodibenzothiazepinyl, dihydropyridobenzothiazepinyl, and oxodihydropyridobenzothiazepinyl, [bound directly or over a methylene group,]

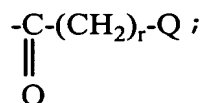
R¹³ has the same meaning as R¹², but is selected independently therefrom,

R¹⁴ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl, indanyl, indenyl, naphthyl, dihydronaphthyl, tetrahydronaphthyl, furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, triazinyl, benzofuryl, benzothienyl, indolyl, indolinyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl, and tetrahydroquinolyl, [bound directly or over a methylene group,]

G2 is selected from the group consisting of



and

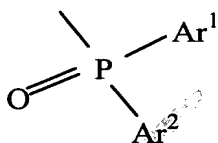
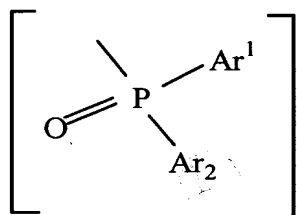


wherein R¹² and R¹⁴ have the above meaning, and Q is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of azetidine, pyrrolidine, piperidine, (1H)tetrahydropyridine, hexahydroazepine, (1H)tetrahydroazepine, octahydroazocine, pyrazolidine, piperazine, hexahydrodiazepine, morpholine, hexahydrooxazepine, thiomorpholine, thiomorpholine-1,1-dioxide, 5-aza-bicyclo[2.1.1]hexane, 2-aza-bicyclo[2.2.1]heptane, 7-aza-bicyclo[2.2.1]heptane, 2,5-diaza-bicyclo[2.2.1]heptane, 2-aza-bicyclo[2.2.2]octane, 8-aza-bicyclo[3.2.1]octane, 2,5-diazabicyclo[2.2.2]octane, 9-azabicyclo[3.3.1]nonane, indoline, isoindoline, (1H)-dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-tetrahydroisoquinoline, (1H)-tetrahydroquinoxaline, (4H)-dihydrobenzoxazine, (4H)-dihydrobenzothiazine, (1H)-tetrahydrobenzo[b]azepine, (1H)-tetrahydrobenzo[c]azepine, (1H)-tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine, (5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole, (10H)-dihydroacridine, 1,2,3,4-tetrahydroacridanone, (10H)-phenoxazine, (10H)-phenothiazine, (5H)-dibenzazepine, (5H)-dihydrodibenzazepine, (5H)-octahydrodibenzazepine, (5H)-dihydrodibenzodiazepine, (11H)-dihydrodibenzo[b,e]oxazepine, (11H)-dihydrodibenzo[b,e]thiazepine, (10H)-dihydrodibenzo[b,f]oxazepine, (10H)-dihydrodibenzo[b,f]thiazepine, and

(5H)-tetrahydrodibenzazocine,

G3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{12}$,

G4 is



wherein

Ar^1 and

Ar^2 are selected independently of each other from the group consisting of phenyl, pyridyl and naphthyl;

G5 is $-\text{COR}^{15}$,

wherein

R^{15} is selected from the group consisting of trifluoromethyl, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy and benzyloxy; and

wherein aromatic rings are substituted or unsubstituted independently of each other by one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, and a substituted C₁-C₆-alkoxy which is entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, [C₁]C₂-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino[, wherein two adjacent groups of an aromatic ring in the substituted C₁-C₆ alkoxy may form an additional ring over a methylenedioxy bridge].

44. (Twice amended) A compound according to claim 43 wherein:

R¹ is selected from the group consisting of hydrogen, halogen, cyano, methyl, trifluoromethyl, hydroxy, methoxy and methoxycarbonyl,

R² is hydrogen or halogen,

R³ is hydrogen,

R⁴ is selected from the group consisting of hydrogen, C₁-C₃-alkyl and hydroxy,

k is 0 or 1,

A is selected from the group consisting of C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once

or twice by hydroxy or fluorine,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted by one or two fluorine atoms, and

1,3,5-hexatrienylene

D is selected from the group consisting of C₂-C₈-alkylene,

a substituted C₂-C₈-alkylene which is substituted by methyl or hydroxy

C₂-C₈-alkenylene,

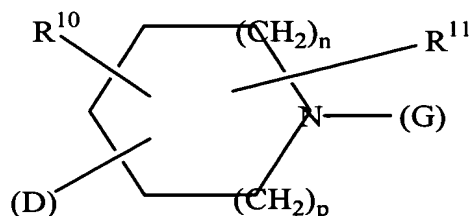
a substituted C₂-C₈-alkenylene which is substituted by methyl or hydroxy,

a C₂-C₈-alkenylene wherein the double bond is to ring E,

a substituted C₂-C₈-alkenylene which is substituted by methyl or hydroxy, wherein the double bond is to ring E,

[an isosterically replaced] a C₂ to C₈ group selected from the group consisting of C₂-C₈-alkylene and C₂-C₈-alkenylene, the [isosterically replaced] C₂ to C₈ group having methylene units [and] wherein one to three of the methylene units are isosterically replaced by O, NH, N(CH₃), N(COCH₃), N(SO₂CH₃) or CO,

E is



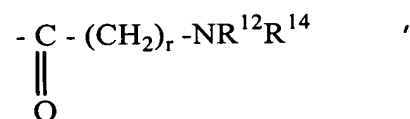
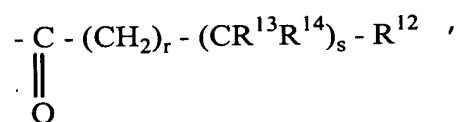
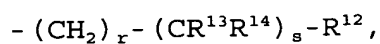
wherein n and p are, independent of each other, 0, 1, 2,

or 3, wherein $n + p \leq 3$,

R^{10} is selected from the group consisting of hydrogen, methyl and hydroxyl,

R^{11} is hydrogen or an oxo group adjacent to the nitrogen atom,

G is selected from the group consisting of hydrogen, C₃-C₈-cycloalkyl, methoxycarbonyl, tert-butoxycarbonyl, benzyloxycarbonyl, trifluoroacetyl, diphenylphosphinoyl,



and



wherein

r is 0, 1 or 2,

s is 0 or 1,

R^{12} is selected from the group consisting of hydrogen,

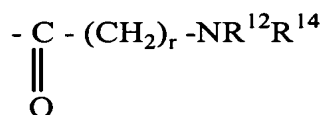
methyly, benzyl, phenyl, indanyl, indenyl, oxoindanyl, naphthyl, dihydronaphthyl, tetrahydronaphthyl, oxotetrahydronaphthyl, flourenyl, oxofluorenyl, anthryl, dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl, dibenzocycloheptenyl, [and] oxodibenzocycloheptenyl, dihydrodibenzocycloheptenyl, oxodihydrodibenzocycloheptenyl bound directly or over a methylene group, furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, imidazothiazolyl, benzofuryl, dihydrobenzofuryl, benzothienyl, dihydrobenzothienyl, indolyl, indolinyl, oxoindolinyl, dioxoindolinyl, benzoxazolyl, oxobenzoxazolyl, benzisoxazolyl, oxobenzisoxazolyl, benzothiazolyl, oxobenzthiazolyl, benzoisothiazolyl, oxobenzoisothiazolyl, benzimidazolyl, oxobenzimidazolyl, benzofurazanyl, benzothiadiaazolyl, benzotriazolyl, oxazolopyridyl, oxodihydrooxazolopyridyl, thiazolopyridyl, oxodihydrothiazolopyridyl, isothiazolopyridyl, imidazopyridyl, oxodihydroimidazopyridyl, pyrazolopyridyl, thienopyrimidinyl, chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl, isoquinolyl, dihydroquinolyl, oxodihydroquinolyl, tetrahydroquinolyl, oxotetrahydroquinolyl, benzodioxanyl, quinoxalyl, quinazolyl, naphthyridyl, carbazolyl, tetrahydrocarbazolyl, oxotetrahydrocarbazolyl, pyridoindolyl, acridyl, oxodihydroacridyl, phenothiazyl, dihydrodibenzoxepinyl, benzocycloheptathienyl, oxobenzocycloheptathienyl, dihydrothienobenzothiepinyl, oxodihydrothienobenzothiepinyl, dihydrodibenzothiepinyl, oxodihydrodibenzothiepinyl, dihydrodibenzazepinyl, oxodihydrodibenzazepinyl, octahydrodibenzazepinyl, benzocycloheptapyridyl, oxobenzocycloheptapyridyl,

dihydropyridobenzoxepinyl, dihydrodibenzothiazepinyl, and oxodihydrodibenzothiazepinyl, [bound directly or over a methylene group,]

R¹³ is selected from the group consisting of hydrogen, methyl, benzyl and phenyl,

R¹⁴ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl, naphthyl, furyl, thienyl, oxazolyl, thiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, pyridyl, benzofuryl, benzothienyl, indolyl, indolinyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl and tetrahydroquinolyl, [bound directly or over a methylene group,]

wherein in formula



-NR¹²R¹⁴ may be selected from the group consisting of pyrrolidine, piperidine, (1H)-tetrahydropyridine, hexahydroazepine, octahydroazocine, piperazine, hexahydrodiazepine, morpholine, hexahydrooxazepine, 2-azabicyclo[2.2.1]heptane, 7-azabicyclo[2.2.1]heptane, 2,5-diazabicyclo[2.2.1]heptane, 8-azabicyclo[3.2.1]octane, 2,5-diazabicyclo[2.2.2]octane, indoline, isoindoline, (1H)-dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-tetrahydroisoquinoline, (1H)-tetrahydroquinoxaline, (4H)-dihydrobenzoxazine, (4H)-dihydrobenzothiazine, (1H)-tetrahydrobenzo[b]azepine, (1H)-tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine, (5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-tetrahydro-9H-

45

pyrido[3,4-b]indole, (10H)-dihydroacridine, 1,2,3,4-tetrahydroacridanone, (5H)-dihydrodibenzazepine, (5H)-dihydrodibenzodiazepine, (11H)-dihydrodibenzo[b,e]oxazepine, (11H)-dihydrodibenzo[b,e]thiazepine, (10H)-dihydrodibenzo[b,f]oxazepine and (5H)-tetrahydrodibenzazocine,

wherein aromatic rings are substituted or unsubstituted independently of each other by one to three substituents independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, and a substituted C₁-C₆-alkoxy entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, {C₁}C₂-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino[, wherein two adjacent groups of an aromatic ring in the substituted C₁-C₆ alkoxy form an additional ring over a methylenedioxy bridge].

45. (Twice amended) A compound according to claim [22] 44, wherein

R¹ is selected from the group consisting of hydrogen, fluorine, chlorine, bromine, methyl, trifluoromethyl and hydroxy,

R² and

R³ are hydrogen,

R⁴ is hydrogen or hydroxy,

k is 0 or 1,

A is selected from the group consisting of C₂-C₄-alkenylene,

1,3-butadienylene,

a C₂-C₄-alkenylene substituted by fluorine, and

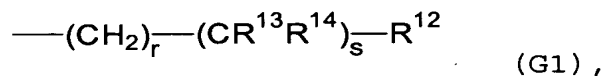
a 1,3-butadienylene substituted by fluorine,

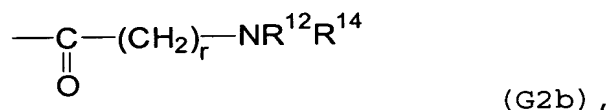
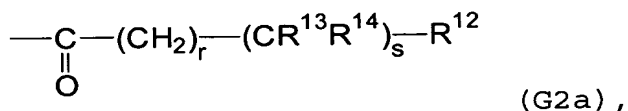
D is selected from the group consisting of C₂-C₆-alkylene, C₂-C₆-alkenylene, [C₂-C₆-alkylene] and C₂-C₆-alkenylene wherein the double bond of the C₂-C₆-alkenylene is to ring E, and

[an isosterically replaced] a C₂ to C₆ group selected from the group consisting of C₂-C₆-alkylene and C₂-C₆-alkenylene, the [isosterically replaced] C₂ to C₆ group having a methylene unit [which] wherein the methylene unit is isosterically replaced by O, NH, N(CH₃) or CO, or the C₂ to C₆ group having an ethylene group which is isosterically replaced by NH-CO or CO-NH, or the C₂ to C₆ group having a propylene group which is isosterically replaced by NH-CO-O or O-CO-NH,

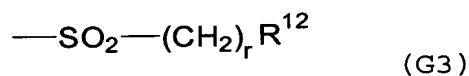
E is selected from the group consisting of piperidine, and a substituted piperidine wherein the heterocyclic ring is substituted by an oxo group adjacent to the nitrogen atom,

G is selected from the group consisting of hydrogen, tert-butoxycarbonyl, diphenylphosphinoyl,





and



wherein

r is 0 or 1,

s is 0 or 1,

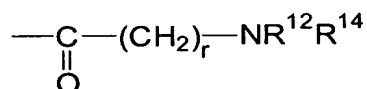
R¹² is selected from the group consisting of hydrogen, methyl, benzyl, phenyl, indenyl, oxoindanyl, naphthyl, tetrahydronaphthyl, fluorenyl, oxofluorenyl, anthryl, dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl, dibenzocycloheptenyl, and dihydrodibenzocycloheptenyl, bound directly or over a methylene group, furyl, thienyl, oxazolyl, thiazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, pyridyl, pyrazinyl, pyrimidinyl, imidazothiazolyl, benzofuryl, benzothienyl, indolyl, oxoindolinyl, dioxoindolinyl, benzoxazolyl, oxobenzoxazolyl, benzothiazolyl, oxobenzthiazolyl, benzimidazolyl, oxobenzimidazolyl, benzofurazanyl, benzotriazolyl, oxazolopyridyl,

oxodihydrooxazolopyridyl, thiazolopyridyl, oxodihydrothiazolopyridyl, chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl, isoquinolyl, oxodihydroquinolyl, tetrahydroquinolyl, oxotetrahydroquinolyl, benzodioxanyl, quinazolinyl, acridinyl, oxodihydroacridinyl, phenothiazinyl, dihydrodibenzoxepinyl, benzocycloheptathienyl, dihydrothienobenzothiepinyl, dihydrodibenzothiepinyl, oxodihydrodibenzothiepinyl, dihydrodibenzazepinyl, oxodihydrodibenzazepinyl, octahydrodibenzazepinyl, benzocycloheptapyridyl, oxobenzocycloheptapyridyl, and dihydrodibenzothiazepinyl, [bound directly or over a methylene group,]

R¹³ is selected from the group consisting of hydrogen, methyl, benzyl and phenyl,

R¹⁴ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl, naphthyl, furyl, thienyl, pyridyl, benzofuryl, benzothienyl, indolyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl and tetrahydroquinolyl, [bound directly or over a methylene group,]

wherein in the formula



(G2b)

---NR¹²R¹⁴ may be selected from pyrrolidine, piperidine,



46

hexahydroazepine, morpholine, 2,5-diazabicyclo[2.2.1]heptane, indoline, isoindoline, (1H)-dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-tetrahydroisoquinoline, (1H)-tetrahydrobenzo[b]azepine, (1H)-tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine, (5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-tetrahydroacridanone, (5H)-dihydrodibenzazepine, (11H)-dihydrodibenzo[b,e]oxazepine and (11H)-dihydrodibenzo[b,e]thiazepine,

wherein aromatic rings are substituted or unsubstituted, independently of each other, by one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, a substituted C₁-C₆-alkoxy which is entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, [C₁]C₂-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino and di-(C₁-C₆-alkyl)-amino[, wherein two adjacent groups on the aromatic ring or ring system may form an additional ring over a methylenedioxy bridge].

46. (Twice amended) A compound according to claim 45, wherein:

R¹ is selected from the group consisting of hydrogen, fluorine, methyl, trifluoromethyl and hydroxy,

R² and

R³ are hydrogen,

R⁴ is hydrogen or hydroxy,

k is 0,

- A is ethenylene or 1,3-butadienylene
- D is selected from the group consisting of C₂-C₆-alkylene, C₂-C₆-alkenylene, [a C₂-C₆-alkylene wherein the double bond is to ring E,] and a C₂-C₆-alkenylene wherein the double bond of the C₂-C₆-alkenylene is to ring E,
- E is selected from the group consisting of pyrrolidine, piperidine, hexahydroazepine and morpholine,
- G is selected from the group consisting of benzyl, phenethyl, fluorenylmethyl, anthrylmethyl, diphenylmethyl, fluorenyl, dihydrodibenzocycloheptenyl, furylmethyl, thienylmethyl, thiazolylmethyl, pyridylmethyl, benzothienylmethyl, quinolylmethyl, phenyl-thienylmethyl, phenyl-pyridylmethyl, dihydrodibenzoxepinyl, dihydrodibenzothiepinyl, acetyl, pivaloyl, phenylacetyl, diphenylacetyl, diphenylpropionyl, naphthylacetyl, benzoyl, naphthoyl, anthrylcarbonyl, oxofluorenylcarbonyl, oxodihydroanthrylcarbonyl, dioxodihydroanthrylcarbonyl, furoyl, pyridylcarbonyl, chromonylcarbonyl, quinolylcarbonyl, naphthylaminocarbonyl, dibenzylaminocarbonyl, benzylphenylaminocarbonyl, diphenylaminocarbonyl, indolinyl-1-carbonyl, dihydrodibenzazepin-N-carbonyl, tetrahydroquinolinyl-N-carbonyl, tetrahydrobenzo[b]azepinyl-N-carbonyl, methanesulfonyl, phenylsulfonyl, p-toluenesulfonyl, naphthylsulfonyl, quinolinsulfonyl, and diphenylphosphinoyl,

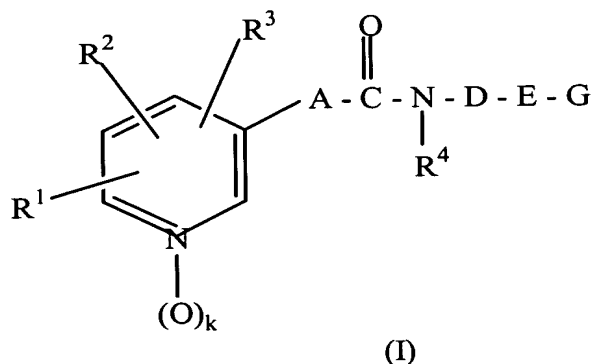
wherein aromatic rings are substituted or unsubstituted



56

independently of each other by one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, C₁-C₆-alkoxy, entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, [C₁]C₂-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups in the ring or ring system may form an additional ring over a methylenedioxy bridge.

56. (Twice amended) A pharmaceutical composition comprising one or more of the compounds according to formula (I) and pharmaceutically acceptable acid addition salts of formula (I)



wherein:

R¹ is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, C₁-C₄-hydroxyalkyl, hydroxy, C₁-C₄-alkoxy, benzyloxy, C₂-C₄-alkanoyloxy, C₁-C₄-alkylthio, C₂-C₅-alkoxycarbonyl, aminocarbonyl, C₃-C₉-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR⁵R⁶, and bridged R¹R²; wherein

R⁵ is selected from the group consisting of hydrogen and C₁-C₆-alkyl; and

R⁶ is selected from the group consisting of hydrogen and C₁-C₆-alkyl;

R² is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and hydroxy and bridged R¹R²;

wherein

bridged R¹R² is where R¹R² are adjacent and form a bridge which is selected from the group consisting of -(CH₂)₄-, $\text{--}(\text{CH}=\text{CH})_2\text{--}$ and -CH₂O-CR⁷R⁸-O-; wherein

R⁷ is selected from the group consisting of hydrogen, and C₁-C₆-alkyl; and

R⁸ is selected from the group consisting of hydrogen and C₁-C₆-alkyl;

R³ is selected from the group consisting of hydrogen, halogen and C₁-C₆-alkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted one to

three-fold by C₁-C₃-alkyl, hydroxy, fluorine, cyano, or phenyl, C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, or cyano, and ethynylene;

D is selected from the group consisting of

C₁-C₁₀-alkylene,

a substituted C₁-C₁₀-alkylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

C₂-C₁₀-alkenylene,

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

a C₂-C₁₀-alkenylene wherein the double bond is to E,

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy, wherein the double bond is to E,

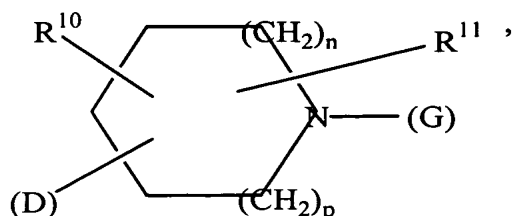
C₃-C₁₀-alkynylene,

a substituted C₃-C₁₀-alkynylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

an isosterically replaced C₁ to C₁₀ group selected from the group consisting of C₁-C₁₀-alkylene, C₂-C₁₀-alkenylene and C₃-C₁₀-alkynylene, the isosterically replaced C₁ to C₁₀ group having methylene units and one to three of the methylene units are isosterically replaced by O, S, NR⁹, CO, SO or SO₂; wherein

R⁹ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, C₂-C₆-acyl and methanesulfonyl;

E is



wherein n and p are, independent of each other, 0, 1, 2, or 3 wherein $n + p \leq 3$,

R^{10} is selected from the group consisting of hydrogen, C_1 - C_3 -alkyl, hydroxy, hydroxymethyl, carboxy and C_2 - C_7 -alkoxycarbonyl;

R^{11} is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen, G1, G2, G3, G4 and G5; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$

wherein

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from the group consisting of
hydrogen,
 C_1 - C_6 -alkyl,
 C_3 - C_6 -alkenyl,

C₃-C₆-alkinyl,
C₃-C₈-cycloalkyl,
benzyl,
phenyl,

monocyclic aromatic five- and six-membered heterocycles which heterocycles contain one to three hetero-atoms selected from the group consisting of N, S and O, [which heterocycles are bound directly to or over a methylene group,]

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring [and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group], and

an [N, S, O] anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from N, S and O [and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group];

R¹³ has the same meaning as R¹², but is selected independently thereof;

R¹⁴ is selected from the group consisting of hydrogen,
hydroxy,
methyl,
benzyl,
phenyl,

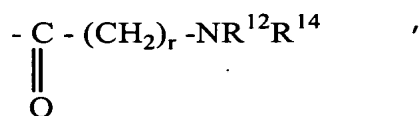
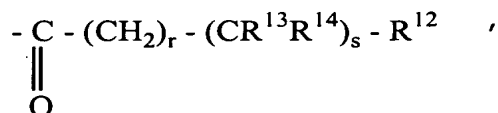
monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O [and are bound either directly

or over a methylene group],

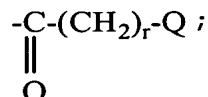
an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring [and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group], and

an [N, S, O] anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms [are] selected from N, S and O [and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group];

G2 is selected from the group consisting of



and



wherein R¹² and R¹⁴ have the above meaning, and Q is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the

group consisting of

saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

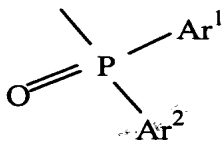
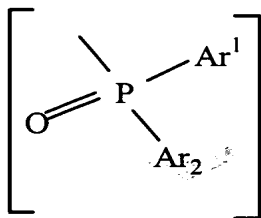
saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms;

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

G3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{12}$,

G4 is





64

wherein

Ar¹ is selected from the group consisting of phenyl, pyridyl and naphthyl; and

Ar² is selected from the group consisting of phenyl, pyridyl and naphthyl;

G5 is -COR¹⁵,

wherein

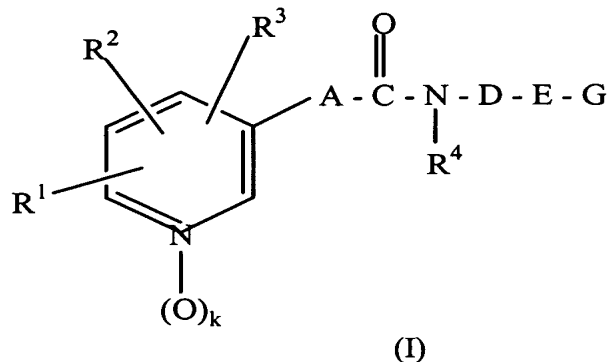
R¹⁵ is selected from the group consisting of trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy and benzyloxy; and

wherein aromatic rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² are unsubstituted or substituted, the substituted rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² having one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, and a substituted C₁-C₆-alkoxy which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, [C₁]C₂-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino, [wherein two adjacent groups of an aromatic ring in the substituted C₁-C₆ alkoxy may form an additional ring over a methylenedioxy bridge,]

wherein general formula (I) does not include (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-2-propenamide.

64. (once amended) A method of inhibiting tumor cell growth in a human or animal body comprising administering to

the human or animal body in need thereof an [effective] amount of a pharmaceutical composition effective for inhibiting tumor cell growth, wherein the pharmaceutical composition includes a compound of general formula (I)



wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_4 -hydroxyalkyl, hydroxy, C_1 - C_4 -alkoxy, benzyloxy, C_2 - C_4 -alkanoyloxy, C_1 - C_4 -alkylthio, C_2 - C_5 -alkoxycarbonyl, aminocarbonyl, C_3 - C_9 -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR^5R^6 , and bridged R^1R^2 ; wherein

R^5 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl; and

R^6 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl;

R^2 is selected from the group consisting of hydrogen, halogen, C_1 - C_6 -alkyl, trifluoromethyl and hydroxy and bridged R^1R^2 ;

wherein

bridged R^1R^2 is where R^1R^2 are adjacent and form a bridge which is selected from the group consisting of $-(CH_2)_4-$, $-(CH=CH)_2-$ and $-CH_2O-CR^7R^8-O-$; wherein

R^7 is selected from the group consisting of hydrogen, and C_1-C_6 -alkyl; and

R^8 is selected from the group consisting of hydrogen and C_1-C_6 -alkyl;

R^3 is selected from the group consisting of hydrogen, halogen and C_1-C_6 -alkyl;

R^4 is selected from the group consisting of hydrogen, C_1-C_6 -alkyl, C_3-C_6 -alkenyl, hydroxy, C_1-C_6 -alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C_2-C_6 -alkenylene,

a substituted C_2-C_6 -alkenylene which is substituted one to three-fold by C_1-C_3 -alkyl, hydroxy, fluorine, cyano, or phenyl,

C_4-C_6 -alkadienylene,

a substituted C_4-C_6 -alkadienylene which is substituted once or twice by C_1-C_3 -alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C_1-C_3 -alkyl, fluorine, or cyano, and ethynylene;

D is selected from the group consisting of C_1-C_{10} -alkylene,

a substituted C_1 - C_{10} -alkylene which is substituted once or twice by C_1 - C_3 -alkyl or hydroxy,

C_2 - C_{10} -alkenylene,

a substituted C_2 - C_{10} -alkenylene which is substituted once or twice by C_1 - C_3 -alkyl or hydroxy,

a C_2 - C_{10} -alkenylene wherein the double bond is to E,

a substituted C_2 - C_{10} -alkenylene which is substituted once or twice by C_1 - C_3 -alkyl or hydroxy, wherein the double bond is to E,

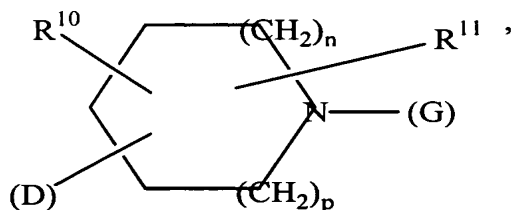
C_3 - C_{10} -alkinylene,

a substituted C_3 - C_{10} -alkinylene which is substituted once or twice by C_1 - C_3 -alkyl or hydroxy,

[an isosterically replaced] a C_1 to C_{10} group selected from the group consisting of C_1 - C_{10} -alkylene, C_2 - C_{10} -alkenylene and C_3 - C_{10} -alkinylene, the [isosterically replaced] C_1 to C_{10} group having methylene units [and] wherein one to three of the methylene units are isosterically replaced by O, S, NR^9 , CO, SO or SO_2 ; wherein

R^9 is selected from the group consisting of hydrogen, C_1 - C_3 -alkyl, C_2 - C_6 -acyl and methanesulfonyl;

E is



wherein n and p are, independent of each other, 0, 1, 2, or 3 wherein $n + p \leq 3$,

R^{10} is selected from the group consisting of hydrogen, C_1 - C_3 -alkyl, hydroxy, hydroxymethyl, carboxy and C_2 - C_7 -alkoxycarbonyl;

R^{11} is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen, G1, G2, G3, G4 and G5; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$

wherein

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from the group consisting of hydrogen,

C_1 - C_6 -alkyl,

C_3 - C_6 -alkenyl,

C_3 - C_6 -alkinyl,

C_3 - C_8 -cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered heterocycles which heterocycles contain one to three hetero-atoms selected from the group consisting of N, S and O, [which heterocycles are bound directly to or over a methylene group,]

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring [and the carbocyclic ring and

aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group], and

a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring[, wherein one to three ring atoms are selected from N, S and O and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group];

R¹³ has the same meaning as R¹², but is selected independently thereof;

R¹⁴ is selected from the group consisting of hydrogen,
hydroxy,
methyl,
benzyl,
phenyl,

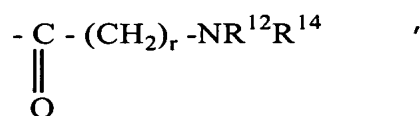
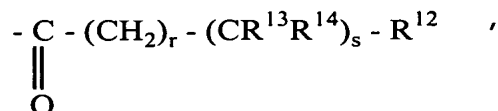
monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O [and are bound either directly or over a methylene group],

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring [and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group], and

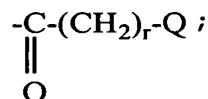
an [N, S, O] anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms [are] selected from N, S and O

[and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group];

G2 is selected from the group consisting of



and



wherein R^{12} and R^{14} have the above meaning, and Q

is a nitrogen-containing heterocycle [bound over the nitrogen atom], the nitrogen-containing heterocycle being selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

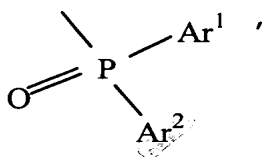
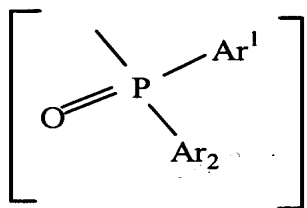
saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms;

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside

from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

G3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{12}$,

G4 is



wherein

Ar^1 is selected from the group consisting of phenyl, pyridyl and naphthyl; and

Ar^2 is selected from the group consisting of phenyl, pyridyl and naphthyl;

G5 is $-\text{COR}^{15}$,

wherein

R^{15} is selected from the group consisting of

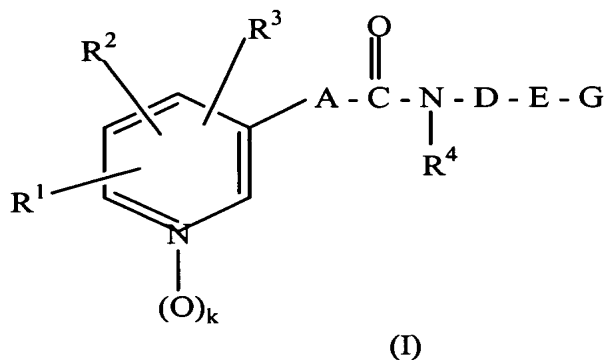


CS

trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy and benzyloxy; and

wherein aromatic rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² are unsubstituted or substituted, the substituted rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² having one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, and a substituted C₁-C₆-alkoxy which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, [C₁] C₂-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino[, wherein two adjacent groups of an aromatic ring in the substituted C₁-C₆ alkoxy may form an additional ring over a methylenedioxy bridge].

65. (Twice amended) A method of suppressing autoimmune disease in a human or animal body comprising administering to the human or animal body in need thereof an [effective] amount of a pharmaceutical composition effective for suppressing autoimmune disease [of], wherein the pharmaceutical composition includes a compound of general formula (I) or a pharmaceutically acceptable acid addition salt of formula (I)



wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_4 -hydroxyalkyl, hydroxy, C_1 - C_4 -alkoxy, benzyloxy, C_2 - C_4 -alkanoyloxy, C_1 - C_4 -alkylthio, C_2 - C_5 -alkoxycarbonyl, aminocarbonyl, C_3 - C_9 -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR^5R^6 , and bridged R^1R^2 ; wherein

R^5 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl; and

R^6 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl;

R^2 is selected from the group consisting of hydrogen, halogen, C_1 - C_6 -alkyl, trifluoromethyl and hydroxy and bridged R^1R^2 ;

wherein

bridged R^1R^2 is where R^1R^2 are adjacent and form a bridge which is selected from the group consisting of $-(CH_2)_4-$, $-(CH=CH)_2-$ and $-CH_2O-CR^7R^8-O-$; wherein

R^7 is selected from the group consisting of hydrogen, and C_1 - C_6 -alkyl; and

R^8 is selected from the group consisting of hydrogen and C_1 - C_6 -alkyl;

R^3 is selected from the group consisting of hydrogen, halogen and C_1 - C_6 -alkyl;

R^4 is selected from the group consisting of hydrogen, C_1 -

C₆-alkyl, C₃-C₆-alkenyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, cyano, or phenyl, C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, or cyano, and ethynylene;

D is selected from the group consisting of

C₁-C₁₀-alkylene,

a substituted C₁-C₁₀-alkylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

C₂-C₁₀-alkenylene,

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

a C₂-C₁₀-alkenylene wherein the double bond is to E,

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy, wherein the double bond is to E,

C₃-C₁₀-alkynylene,

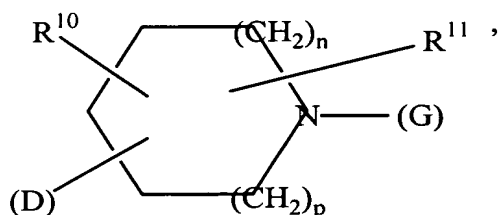
a substituted C₃-C₁₀-alkynylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

[an isosterically replaced] a C₁ to C₁₀ group selected from the group consisting of C₁-C₁₀-alkylene, C₂-C₁₀-alkenylene and C₃-C₁₀-alkynylene, the [isosterically replaced] C₁ to C₁₀

group having methylene units [and] wherein one to three of the methylene units are isosterically replaced by O, S, NR⁹, CO, SO or SO₂; wherein

R⁹ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, C₂-C₆-acyl and methanesulfonyl;

E is



wherein n and p are, independent of each other, 0, 1, 2, or 3 wherein $n + p \leq 3$,

R¹⁰ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, hydroxy, hydroxymethyl, carboxy and C₂-C₇-alkoxycarbonyl;

R¹¹ is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen,

G1, G2, G3, G4 and G5; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$

wherein

r is 0, 1 or 2, and

s is 0 or 1,

R¹² is selected from the group consisting of

hydrogen,

C₁-C₆-alkyl,

C₃-C₆-alkenyl,

C₃-C₆-alkinyl,

C₃-C₈-cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered heterocycles which heterocycles contain one to three hetero-atoms selected from the group consisting of N, S and O, which heterocycles are bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

an [N, S, O] anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from N, S and O and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group;

R¹³ has the same meaning as R¹², but is selected independently thereof;

R¹⁴ is selected from the group consisting of hydrogen, hydroxy,

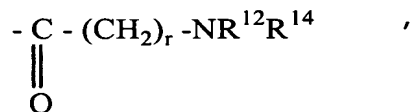
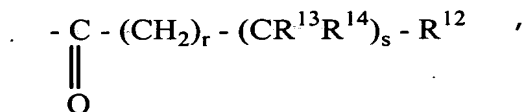
methyl,
benzyl,
phenyl,

monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

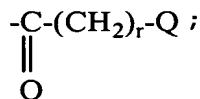
an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

an [N, S, O] anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms [are] selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group;

G2 is selected from the group consisting of



and



wherein R^{12} and R^{14} have the above meaning, and Q

is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

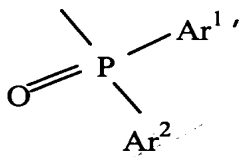
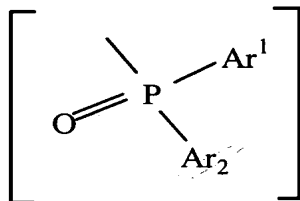
saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms;

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

G3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{12}$,

G4 is





66

wherein

Ar¹ is selected from the group consisting of phenyl, pyridyl and naphthyl; and

Ar² is selected from the group consisting of phenyl, pyridyl and naphthyl;

G5 is -COR¹⁵,

wherein

R¹⁵ is selected from the group consisting of trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy and benzyloxy; and

wherein aromatic rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² are unsubstituted or substituted, the substituted rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² having one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₆-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, C₁-C₆-alkoxy, and a C₁-C₆ alkoxy which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, [C₁]C₂-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino[, wherein two adjacent groups of an aromatic ring in the substituted C₁-C₆ alkoxy may form an additional ring over a methylenedioxy bridge]

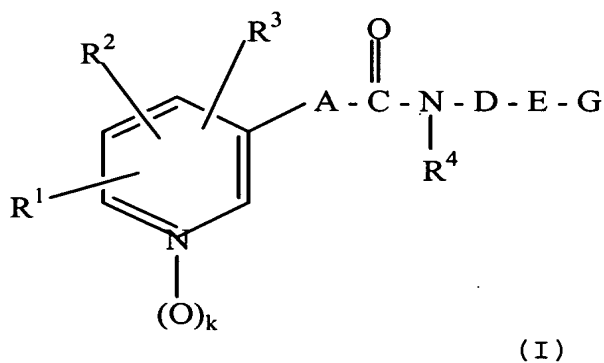
66. (Once amended) A method of [treating cancer] inhibiting tumor cell growth in [the] a human or animal body comprising administering to the human or animal body in need thereof an [effective] amount of a pharmaceutical composition

68

effective for inhibiting tumor cell growth, the pharmaceutical composition comprising (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidine-4-yl)ethyl]-2-propenamide hydrochloride [as active ingredient, optionally together with a pharmaceutically acceptable carrier, a toxicologically safe adjuvant, and optionally in combination with other active ingredients].

67. (Once amended) A method of suppressing autoimmune reactions in the human or animal body comprising administering to the human or animal body in need thereof an [effective] amount of a pharmaceutical composition effective for suppressing autoimmune reactions, the pharmaceutical composition comprising (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidine-4-yl)ethyl]-2-propenamide hydrochloride [as active ingredient, optionally together with a pharmaceutically acceptable carrier, a toxicologically safe adjuvant, and optionally in combination with other active ingredients].

68. (once amended) A compound of formula (I) and pharmaceutically acceptable acid addition salts of formula (I)



wherein:

R¹ is selected from the group consisting of hydrogen, fluorine, chlorine, bromine, methyl, trifluoromethyl and

hydroxy,

R^2 and R^3 are hydrogen,

R^4 is hydrogen or hydroxy,

k is 0 or 1,

A is selected from the group consisting of C_2 - C_4 -alkenylene,

a substituted C_2 - C_4 -alkenylene which is substituted with fluorine,

1,3-butadienylene, and

a substituted 1,3-butadienylene which is substituted with fluorine,

D is selected from the group consisting of C_2 - C_6 -alkylene,

a C_2 - C_6 -alkenylene wherein the double bond is to E,

a substituted C_2 - C_6 -alkenylene which is substituted once or twice by C_1 - C_3 -alkyl or hydroxy, and

an isosterically replaced C_2 - C_6 -alkylene wherein a methylene unit of the alkenylene is isosterically replaced by O, NH, $N(CH_3)$ or CO, or a C_2 - C_6 -alkylene wherein an ethylene group of the alkenylene is isosterically replaced by NH-CO or CO-NH, or a C_2 - C_6 -alkylene wherein a propylene group of the alkenylene is isosterically replaced by NH-CO-O or O-CO-NH,

E is selected from pyrrolidine, piperidine, 1,2,5,6-tetrahydropyridine, hexahydroazepine, morpholine and hexahydro-1,4-oxazepine,

G is selected from the group consisting of hydrogen,

tert-butoxycarbonyl, diphenylphosphinoyl,

$-(\text{CH}_2)_r - (\text{CR}^{13}\text{R}^{14})_s - \text{R}^{12}$,

$-\overset{\text{O}}{\underset{\parallel}{\text{C}}} - (\text{CH}_2)_r - (\text{CR}^{13}\text{R}^{14})_s - \text{R}^{12}$,

$-\overset{\text{O}}{\underset{\parallel}{\text{C}}} - (\text{CH}_2)_r - \text{NR}^{12}\text{R}^{14}$,

$-\text{SO}_2 - (\text{CH}_2)_r \text{R}^{12}$,

and

$-\overset{\text{O}}{\underset{\parallel}{\text{C}}} - (\text{CH}_2)_r - \text{Q}$

wherein r is 0 or 1, and

s is 0 or 1,

R^{12} is selected from the group consisting of hydrogen, [hydrogen,] methyl, benzyl, phenyl, indenyl, oxoindanyl, naphthyl, tetrahydronaphthyl, fluorenyl, oxofluorenyl, anthryl, dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl, [and] dibenzocycloheptenyl, dihydrodibenzocycloheptenyl, furyl, thienyl, oxazolyl, thiazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, pyridyl, pyrazinyl, pyrimidinyl, imidazothiazolyl, benzofuryl, benzothienyl, indolyl, oxoindolinyl, dioxoindolinyl, benzoxazolyl, oxobenzoxazolyl, benzothiazolyl, oxobenzthiazolyl, benzimidazolyl, oxobenzimidazolyl,

benzofurazanyl, benzotriazolyl, oxazolopyridyl, oxodihydrooxazolopyridyl, thiazolopyridyl, oxodihydrothiazolopyridyl, chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl, isoquinolyl, oxodihydroquinolyl, tetrahydroquinolyl, oxotetrahydroquinolyl, benzodioxanyl, quinazolinyl, acridinyl, oxodihydroacridinyl, phenothiazinyl, dihydrodibenzoxepinyl, benzocycloheptathienyl, dihydrothienobenzothiepinyl, dihydrodibenzothiepinyl, oxodihydrodibenzothiepinyl, dihydrodibenzazepinyl, oxodihydrodibenzazepinyl, octahydrodibenzazepinyl, benzocycloheptapyridyl, oxobenzocycloheptapyridyl, and dihydrodibenzothiazepinyl,

R¹³ is selected from the group consisting of hydrogen, methyl, benzyl or and phenyl,

R¹⁴ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl, and

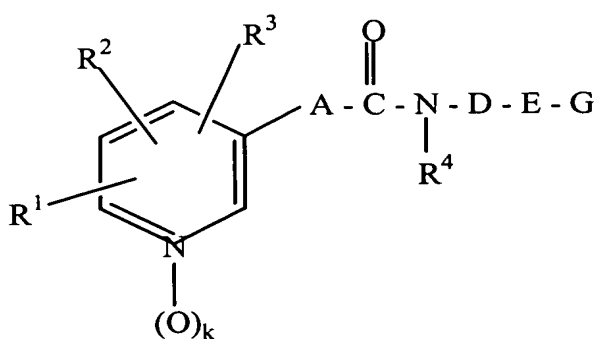
the group consisting of naphthyl, furyl, thienyl, pyridyl, benzofuryl, benzothienyl, indolyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl and tetrahydroquinolyl,

wherein Q is selected from the group consisting of pyrrolidine, piperidine, hexahydroazepine, morpholine, 2,5-diazabicyclo[2.2.1]heptane, indoline, isoindoline, (1H)-dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-tetrahydroisoquinoline, (1H)-tetrahydrobenzo[b]azepine, (1H)-tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine, (5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-tetrahydroacridanone, (5H)-dihydrodibenzazepine, (11H)-dihydrodibenzo[b,e]oxazepine and (11H)-

69

dihydrodibenzo[b,e]thiazepine, wherein general formula (I) does not include (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-2-propenamide.

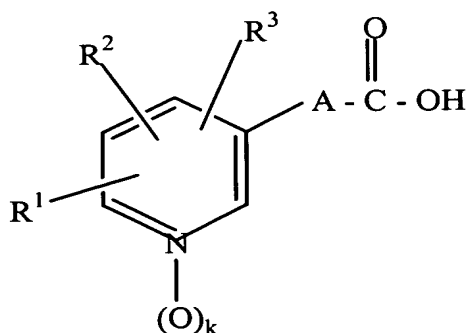
69. (Once amended) A method for the production of compounds having general formula (I)



(I)

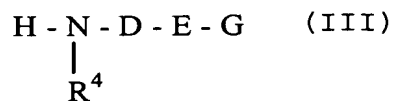
the method comprising:

reacting a carboxylic acids of formula (II)



(II)

with compounds of formula (III)



wherein

R¹ is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, C₁-C₄-hydroxyalkyl, hydroxy, C₁-C₄-alkoxy, benzyloxy, C₂-C₄-alkanoyloxy, C₁-C₄-alkylthio, C₂-C₅-alkoxycarbonyl, aminocarbonyl, C₃-C₉-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR⁵R⁶, and bridged R¹R² wherein

R⁵ is selected from the group consisting of hydrogen and C₁-C₆-alkyl, and

R⁶ is selected from the group consisting of hydrogen and C₁-C₆-alkyl,

R² is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and hydroxy and bridged R¹R²

wherein

bridged R¹R² is where R¹R² are adjacent and form a bridge which is selected from the group consisting of -(CH₂)₄-, -(CH=CH)₂- and -CH₂O-CR⁷R⁸-O-, wherein

R⁷ is selected from the group consisting of hydrogen, and C₁-C₆-alkyl and

R⁸ is selected from the group consisting of hydrogen and C₁-C₆-alkyl,

R³ is selected from the group consisting of hydrogen, halogen and C₁-C₆-alkyl,

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, hydroxy, C₁-C₆-alkoxy and benzyloxy,

k is 0 or 1,

A is selected from the group consisting of C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, cyano, or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano, or phenyl,

1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, or cyano, and ethynylene,

D is selected from the group consisting of

C₁-C₁₀-alkylene,

a substituted [1,3,5-hexatrienylene] C₁-C₁₀-alkylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

C₂-C₁₀-alkenylene,

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

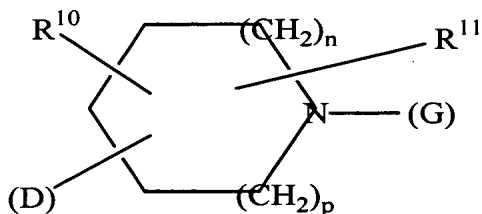
C₃-C₁₀-alkynylene,

a substituted C₃-C₁₀-alkynylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

an isosterically replaced C_1 to C_{10} group selected from the group consisting of C_1 - C_{10} -alkylene, C_2 - C_{10} -alkenylene and C_3 - C_{10} -alkynylene, the isosterically replaced C_1 to C_{10} group having methylene units and one to three of the methylene units are isosterically replaced by O, S, NR^9 , CO, SO or SO_2 , wherein

R^9 is selected from [selected from] the group consisting of hydrogen, C_1 - C_3 -alkyl, C_2 - C_6 -acyl and methanesulfonyl,

E is



wherein n and p are, independent of each other, 0, 1, or 2, wherein $n + p = 2$,

R^{10} is selected from the group consisting of hydrogen, C_1 - C_3 -alkyl, hydroxy, hydroxymethyl, carboxy and C_2 - C_7 -alkoxycarbonyl,

R^{11} is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E,

G is selected from the group consisting of hydrogen, G1, G2, G3, G4 and G5, wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$

wherein

r is 0, 1 or 2, and

s is 0 or 1,

R¹² is selected from the group consisting of
hydrogen,
C₁-C₆-alkyl,
C₃-C₆-alkenyl,
C₃-C₆-alkinyl,
C₃-C₈-cycloalkyl,
benzyl,
phenyl,

monocyclic aromatic five- and six-membered heterocycles which heterocycles contain one to three hetero-atoms selected from the group consisting of N, S and O, the N, S and O being either bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carboxylic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

an ~~[N, S, O]~~ anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from N, S and O and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group,

R¹³ has the same meaning as R¹², but is selected independently thereof,

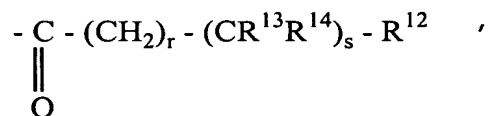
R¹⁴ is selected from the group consisting of hydrogen,
hydroxy,
methyl,
benzyl,
phenyl,

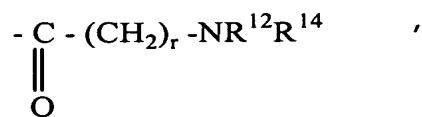
monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

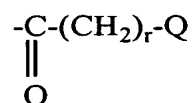
an [N, S, O] anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms [are] selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group,

G2 is selected from the group consisting of





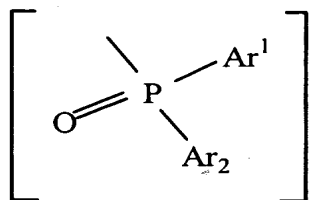
and



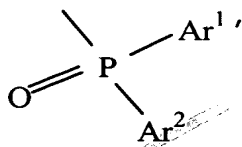
wherein R^{12} and R^{14} have the above meaning, and Q is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of saturated and unsaturated monocyclic, four- to eight-membered heterocycles, and saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms,

G3 is $\text{---SO}_2\text{---}(\text{CH}_2)_r\text{---R}^{12}$,

G4 is



70



wherein

Ar¹ is selected from the group consisting of phenyl, pyridyl and naphthyl and

Ar² is selected from the group consisting of phenyl, pyridyl and naphthyl,

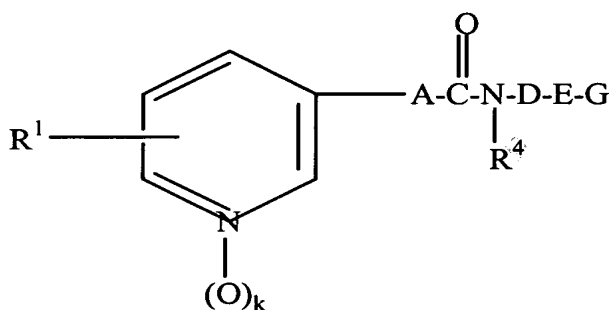
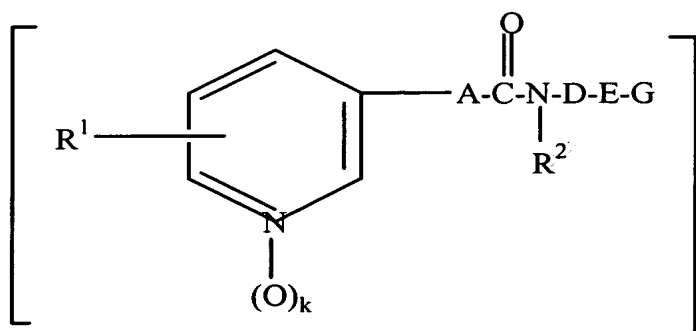
G5 is -COR¹⁵,

wherein

R¹⁵ is selected from the group consisting of trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy and benzyloxy, and

wherein aromatic rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² are unsubstituted or substituted, the substituted rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² having one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, and C₁-C₆-alkoxy.

70. (Once amended) A compound of formula (I) and pharmaceutically acceptable acid addition salts of formula I



wherein:

$R^1 = \text{H or F}$

k is 0 or 1,

A is selected from the group consisting of C_2 - C_6 -alkenylene,

a substituted C_2 - C_6 -alkenylene which is substituted one to three-fold by C_1 - C_3 -alkyl, hydroxy, fluorine, cyano, or phenyl, [C_4 - C_6 -alkenylene,]

a substituted C_4 - C_6 -alkadienylene which is substituted once or twice by C_1 - C_3 -alkyl, fluorine, cyano, or phenyl,

1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, or cyano, and ethynylene;

[R²] R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

D is selected from the group consisting of C₁-C₁₀-alkylene,

a substituted [1,3,5-hexatrienylene] C₁-C₁₀-alkylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

C₂-C₁₀-alkenylene,

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

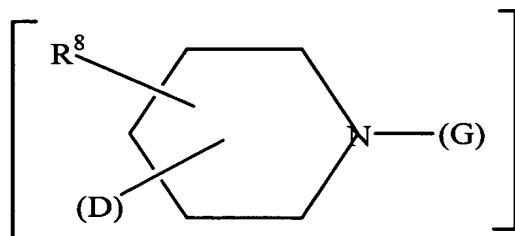
C₃-C₁₀-alkynylene,

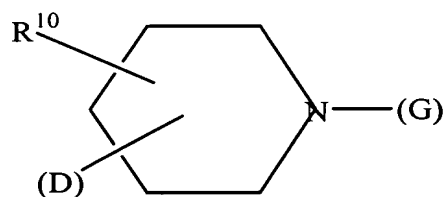
a substituted C₃-C₁₀-alkynylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

an isosterically replaced C₁ to C₁₀ group selected from the group consisting of C₁-C₁₀-alkylene, C₂-C₁₀-alkenylene and C₃-C₁₀-alkynylene, the isoterically replaced C₁ to C₁₀ group having methylene units and one to three of the methylene units being isosterically replaced by O, S, [NR³,] NR⁹, CO, SO or SO₂;

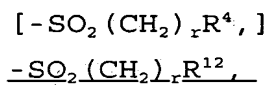
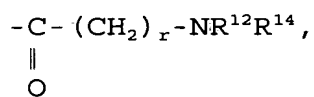
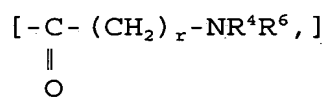
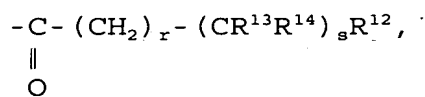
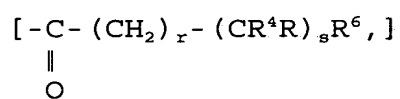
[R³] R⁹ is selected from [selected from] the group consisting of hydrogen, C₁-C₃-alkyl, C₂-C₆-acyl and methanesulfonyl;

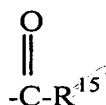
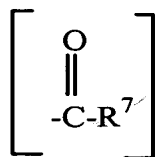
E is





G is selected from the group consisting of
 $[-(\text{CH}_2)_r - (\text{CR}^4\text{R}^6)_s\text{R}^5]$ $-(\text{CH}_2)_r - (\text{CR}^{13}\text{R}^{14})_s\text{R}^{12}$,





$r=0, 1 \text{ or } 2,$

$s=0 \text{ or } 1,$

[R⁴] R¹² is selected from the group consisting of hydrogen, C₁-C₆ alkyl, C₃-C₆ alkenyl, [C₃-C₆ alkenyl,] C₃-C₈-cycloalkyl, benzyl phenyl, and substituted phenyl which substituted phenyl is substituted with one to three substituents selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, and C₁-C₆-alkoxy;

[R⁵] R¹³ is selected from the group consisting of hydrogen, C₁-C₆ alkyl, C₃-C₆ alkenyl, C₃-C₆ alkenyl, C₃-C₈-cycloalkyl, benzyl phenyl, and substituted phenyl which substituted phenyl is substituted with one to three substituents selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, and C₁-C₆-alkoxy;

[R⁶] R¹⁴ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, and phenyl;

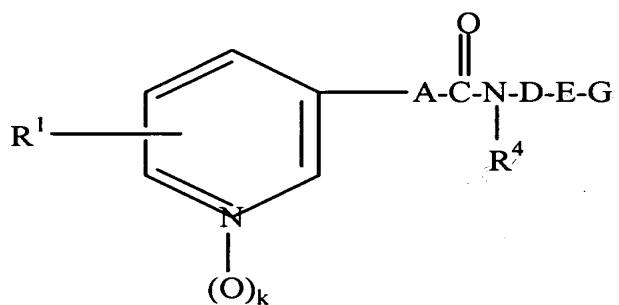
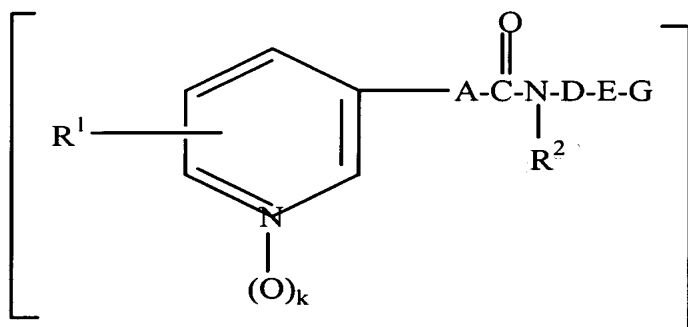
[R⁷] R¹⁵ is selected from trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy and benzyloxy;

71

[R⁸] R¹⁰ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, hydroxy, hydroxymethyl, carboxy and C₂-C₇-alkoxycarbonyl;

and wherein general formula (I) does not include (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-2-propenamide.

71. (Once amended) A compound of formula (I) and pharmaceutically acceptable acid addition salts of formula (I)



wherein:

R^1 is selected from the group consisting of hydrogen, fluorine, chlorine, methoxy, methyl, and hydroxy;

[R^2 and R^3 are hydrogen;]

R^4 is hydrogen, methyl or hydroxy;

k is 0 or 1;

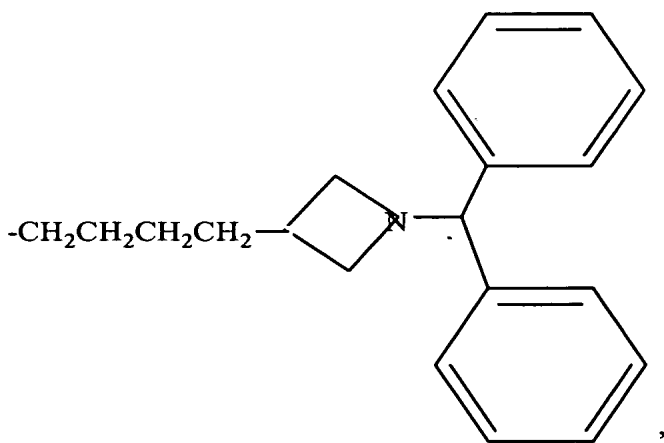
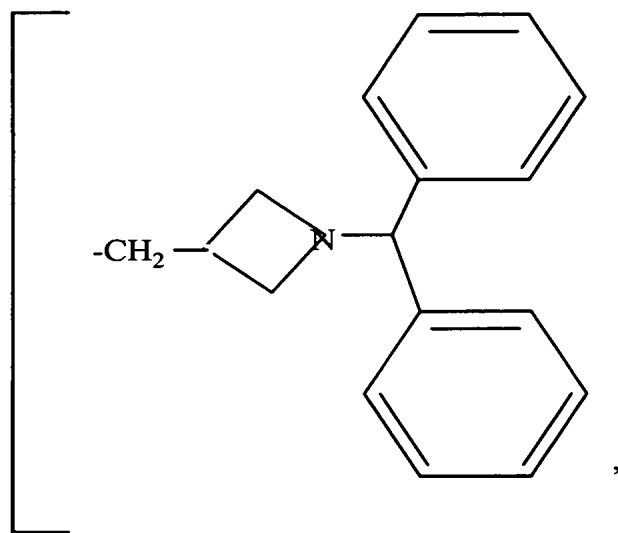
A is selected from the group consisting of C_2 - C_4 -alkenylene,

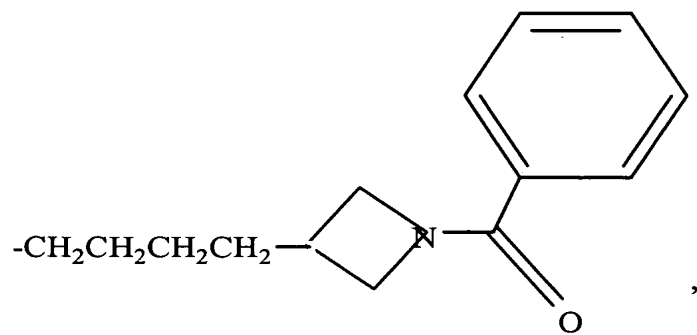
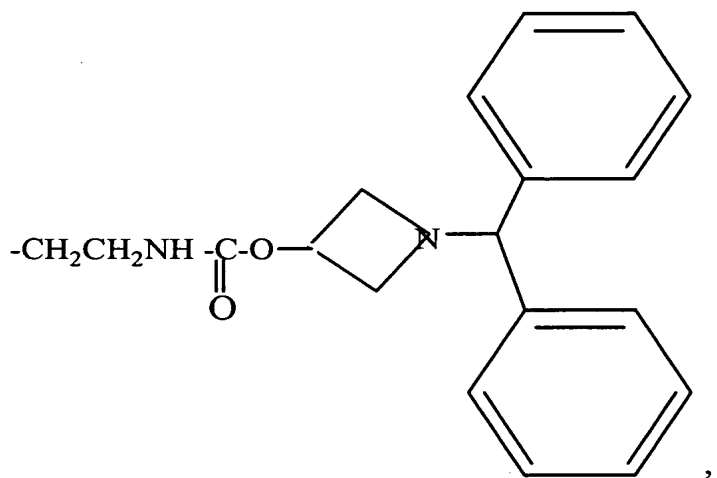
a substituted C_2 - C_4 -alkenylene which is substituted with fluorine, cyano, hydroxy and methyl,

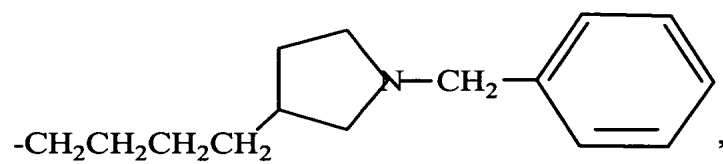
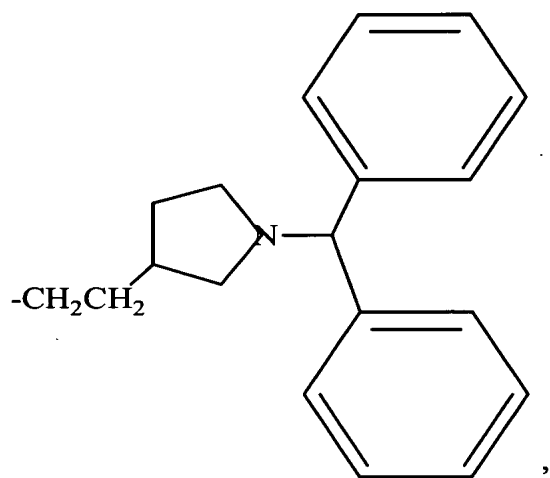
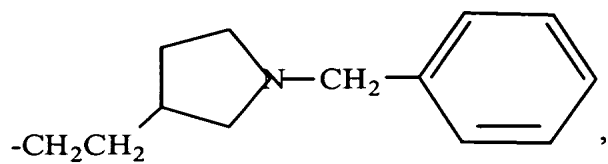
1,3-butadienylene, and

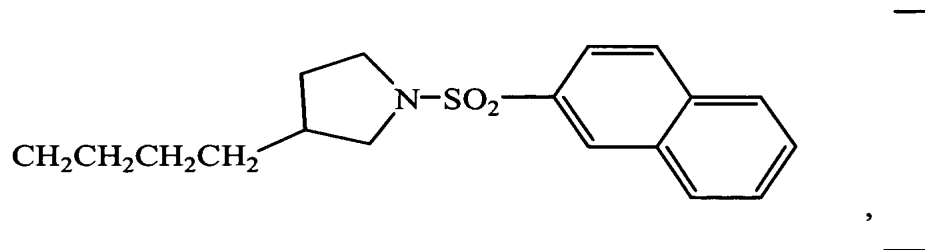
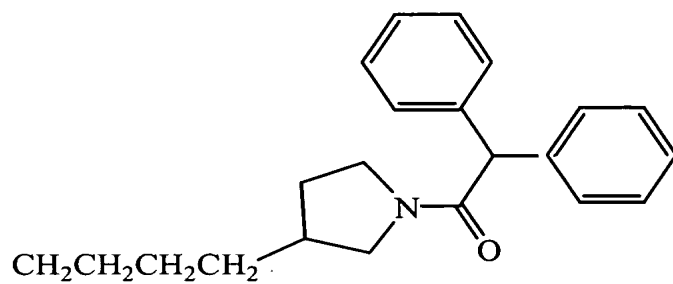
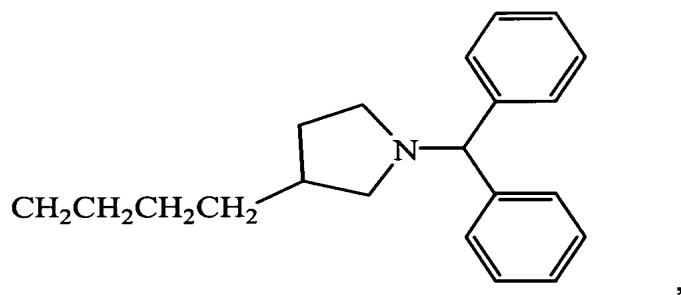
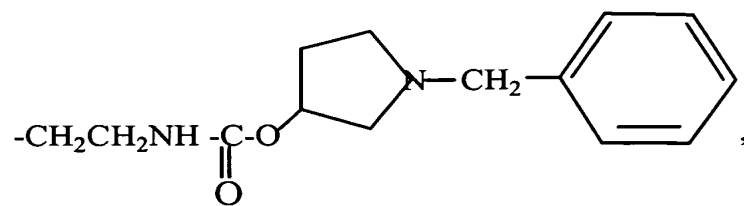
a substituted 1,3-butadienylene which is substituted with fluorine;

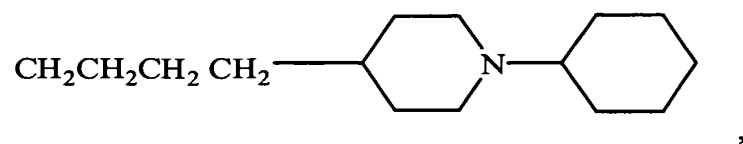
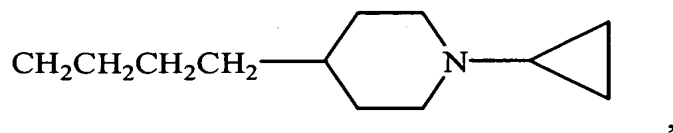
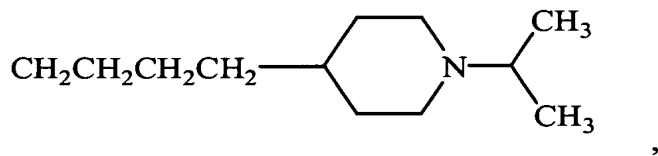
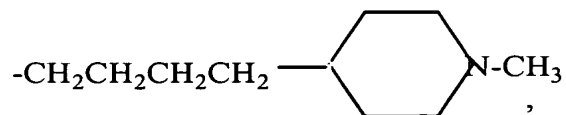
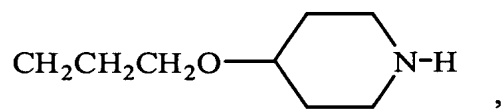
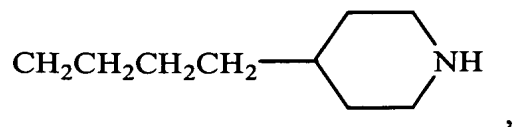
DEG when together form the structure selected from the group consisting of

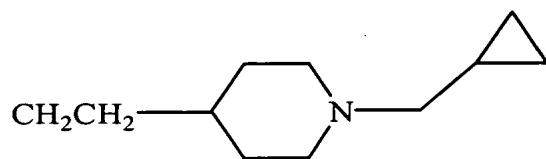




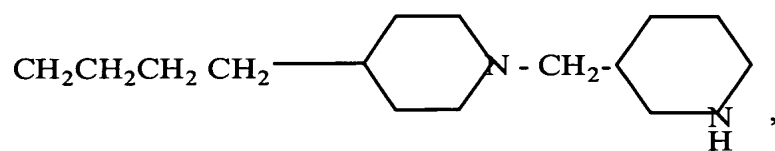




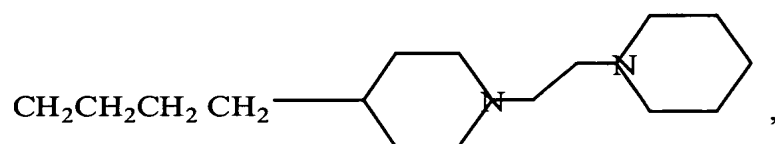




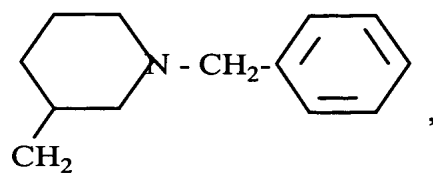
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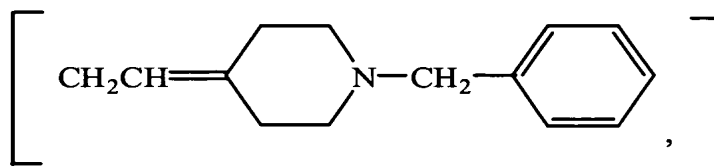
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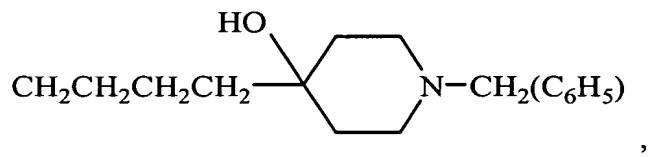
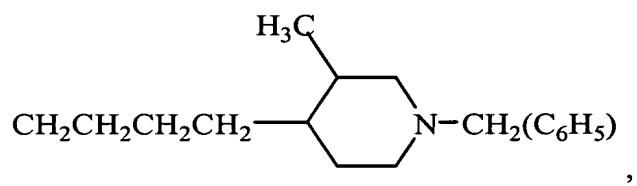
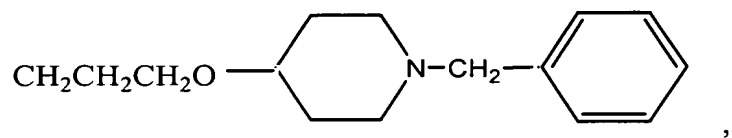
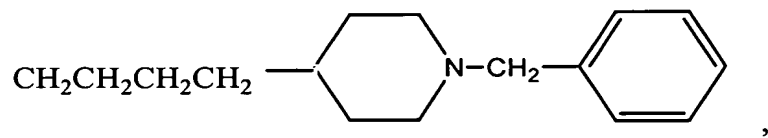
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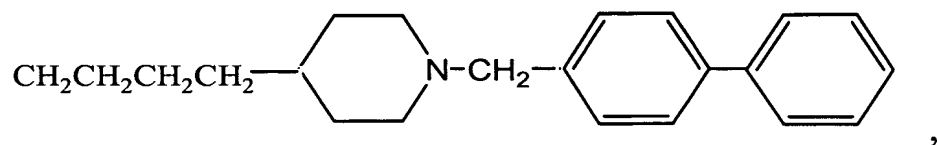
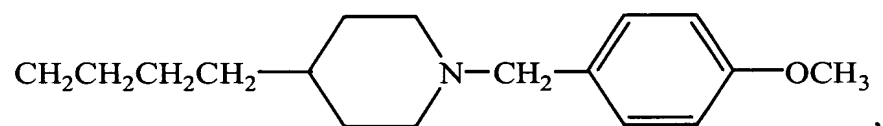
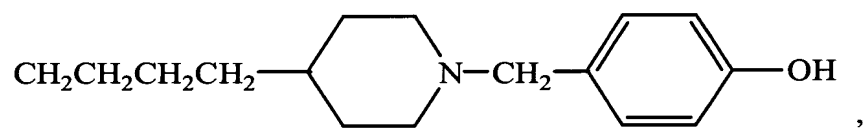
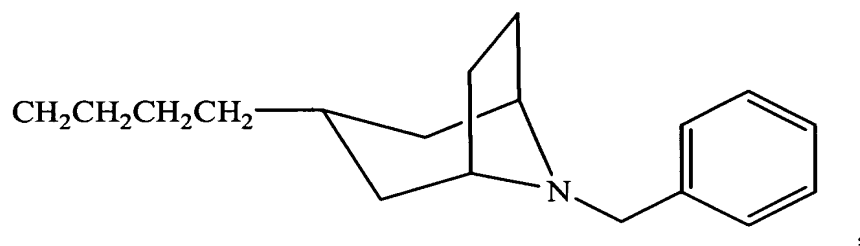
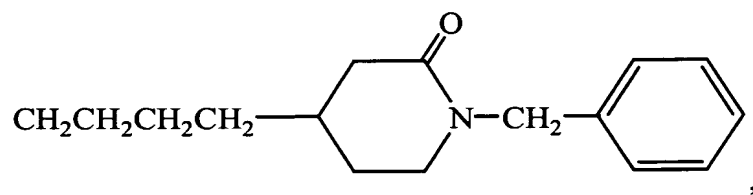


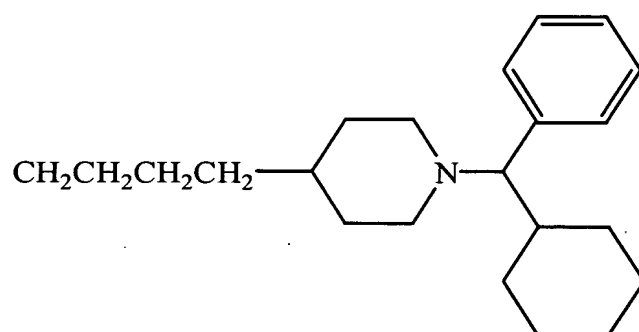
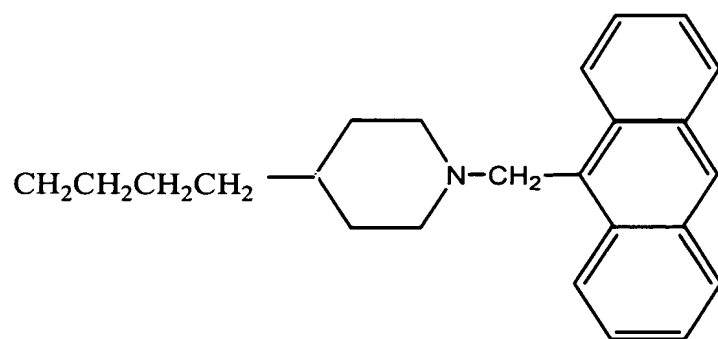
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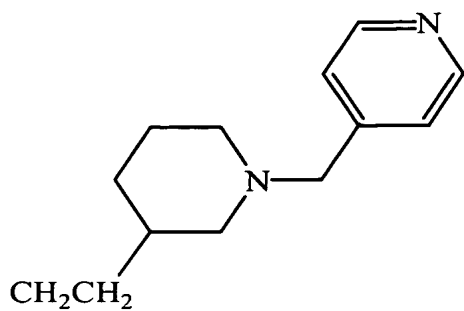


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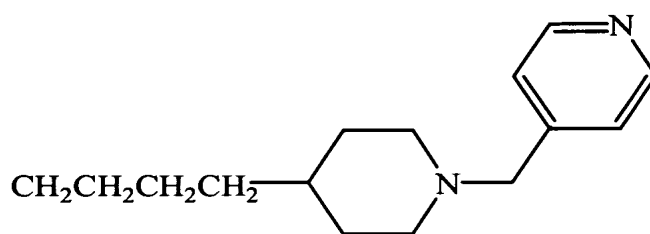




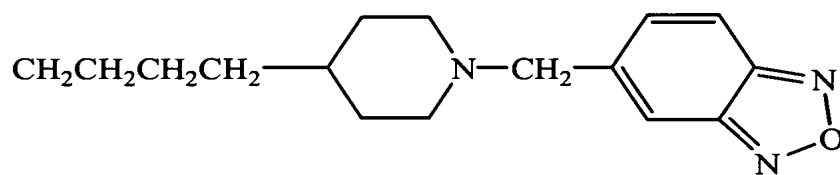




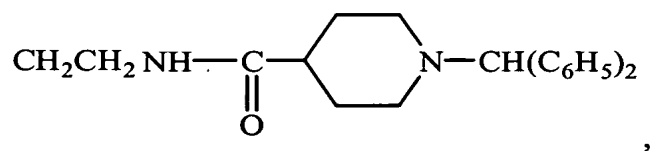
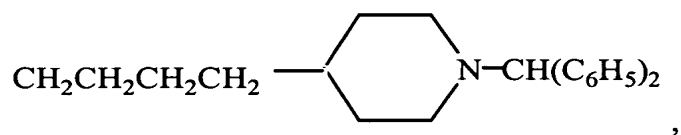
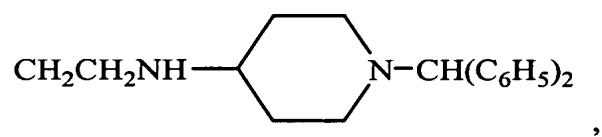
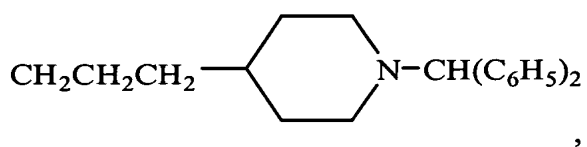
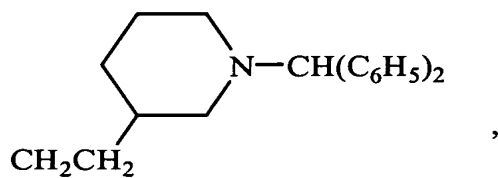
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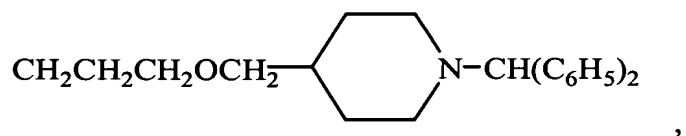
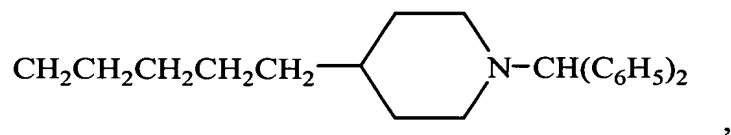
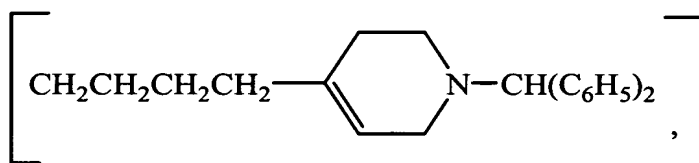
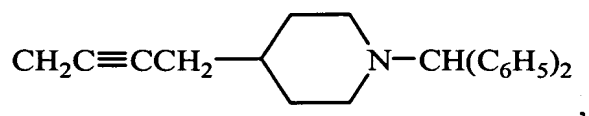
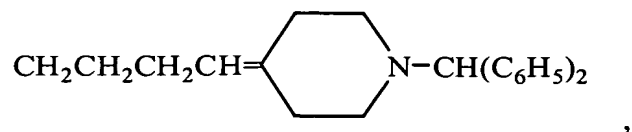


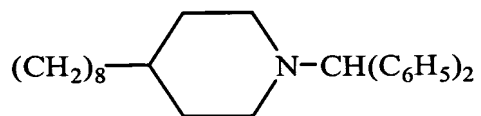
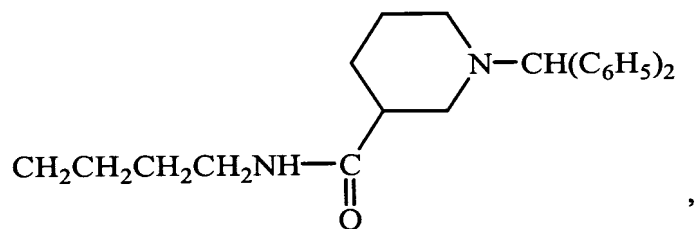
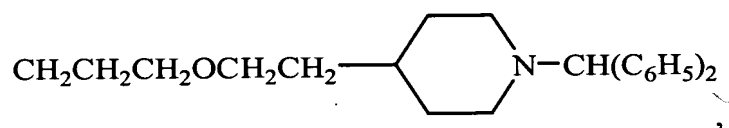
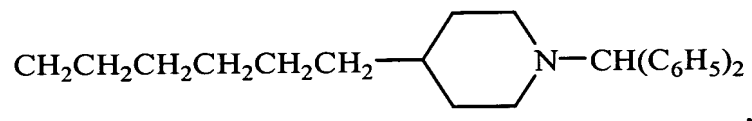
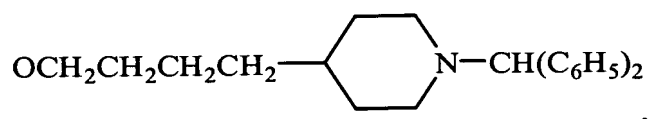
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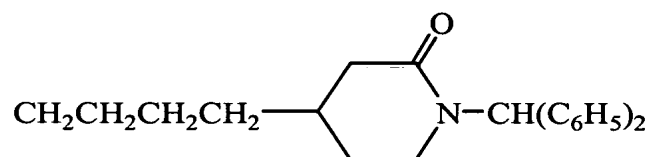
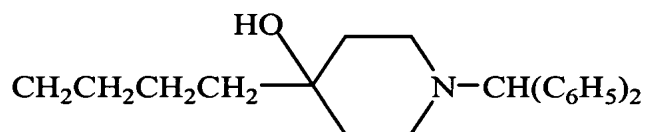
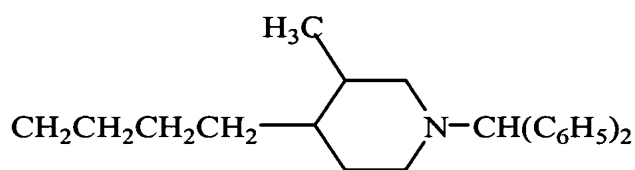
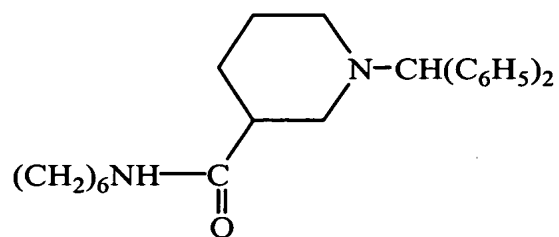


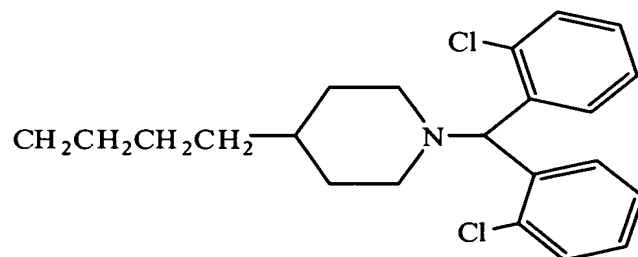
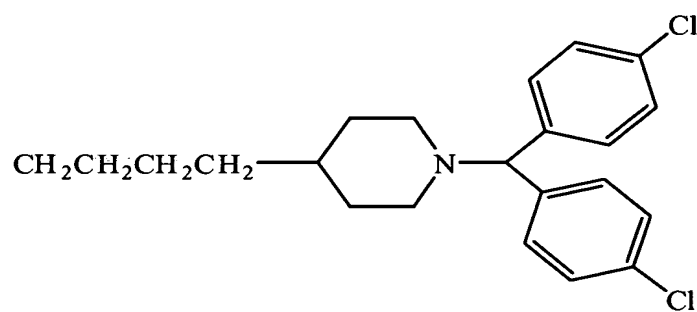
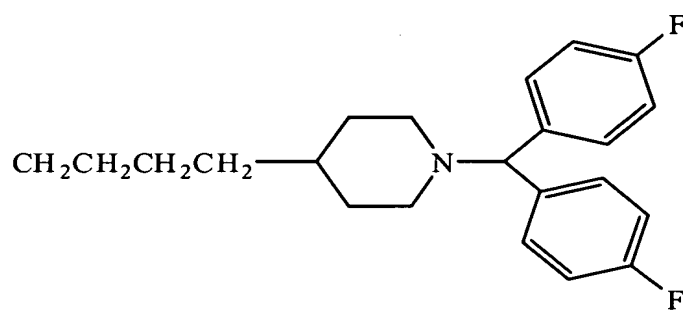
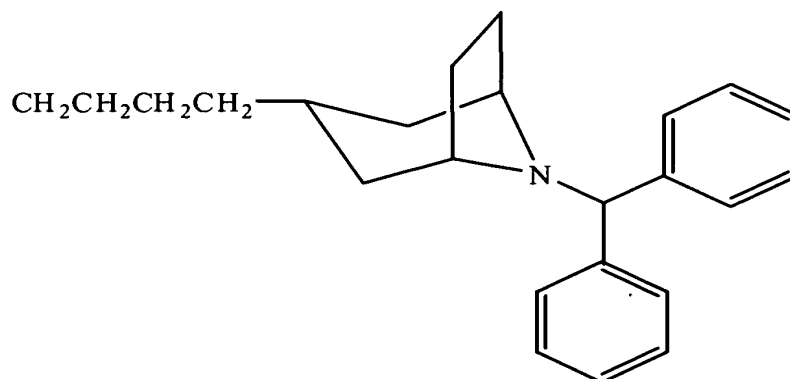
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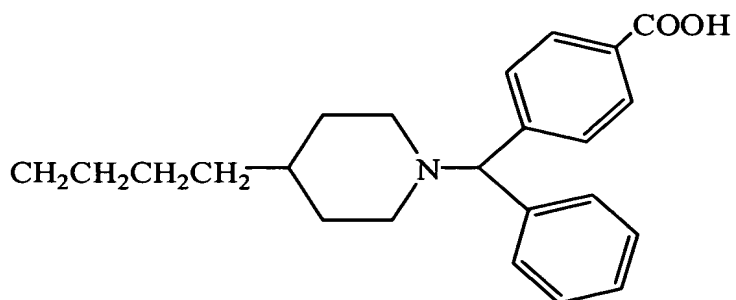
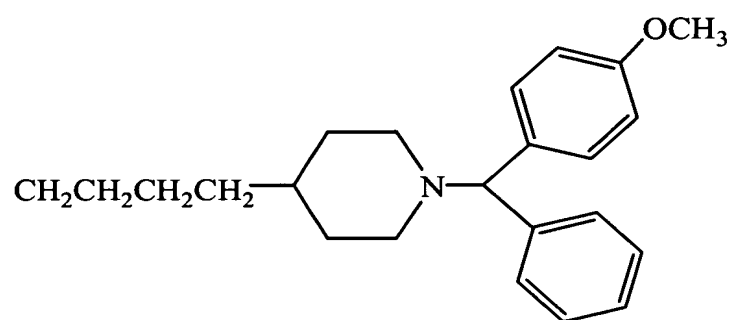
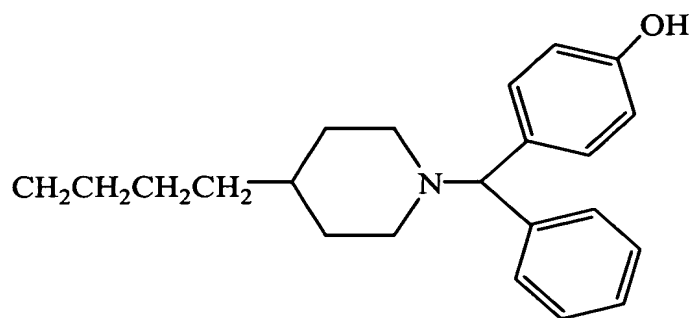


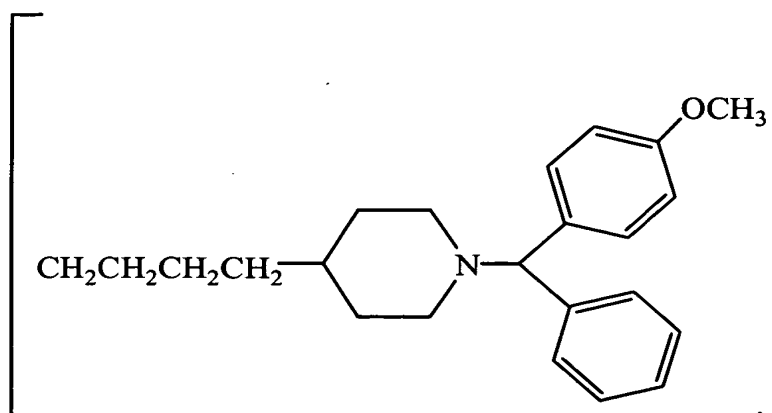
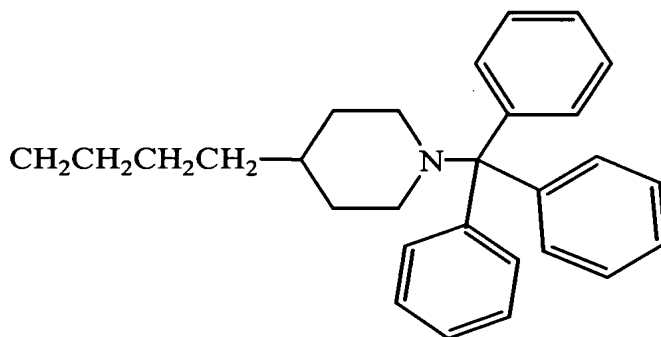
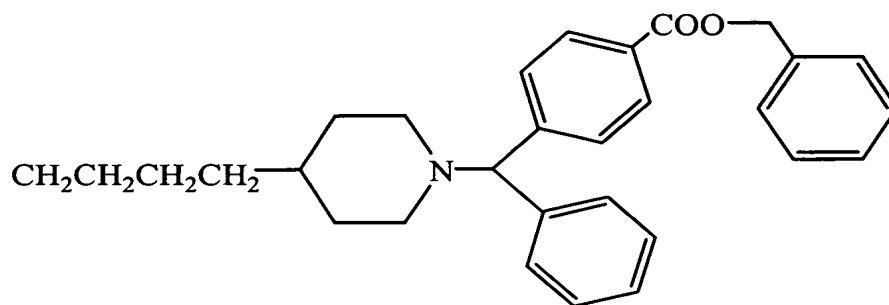


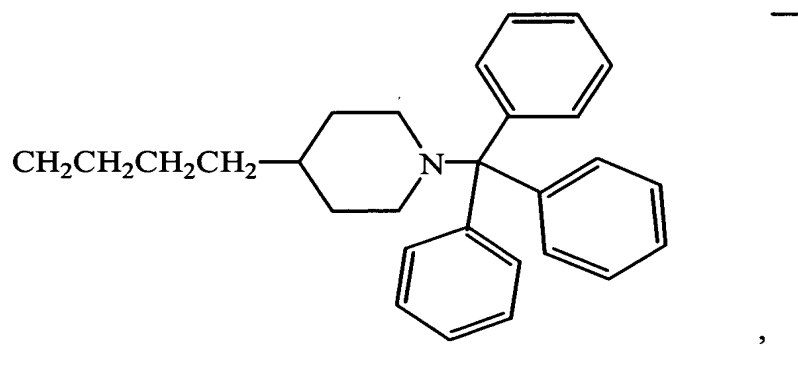
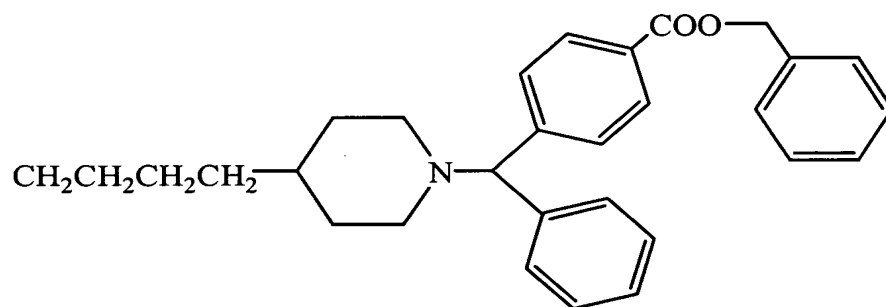
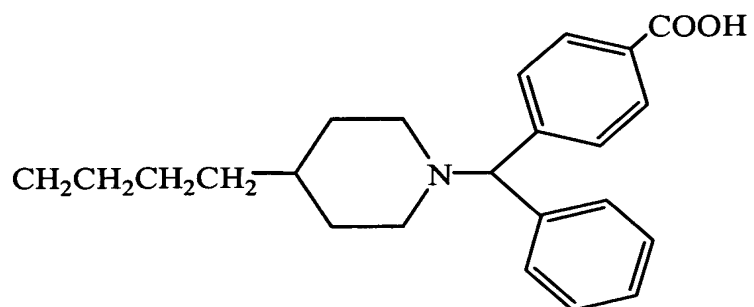


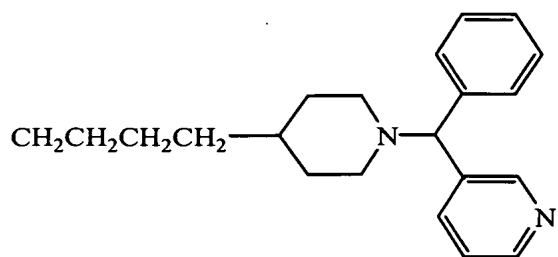




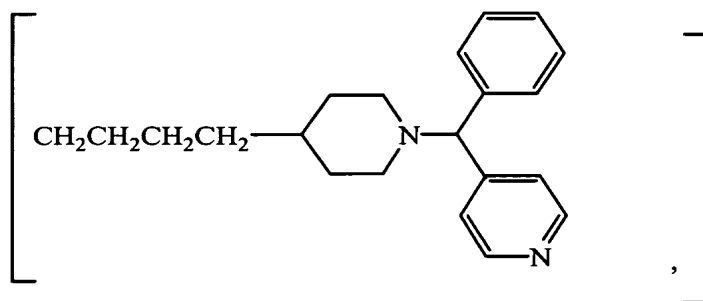




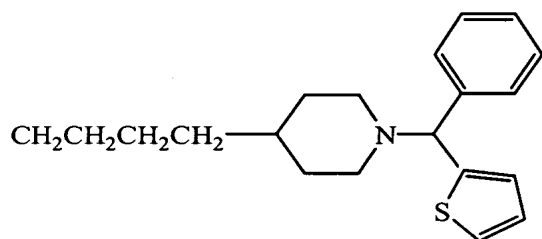




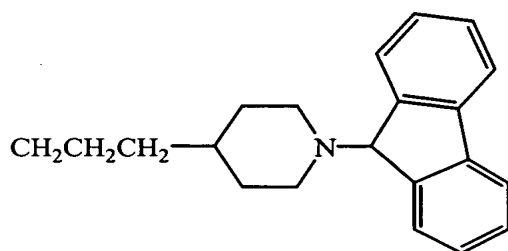
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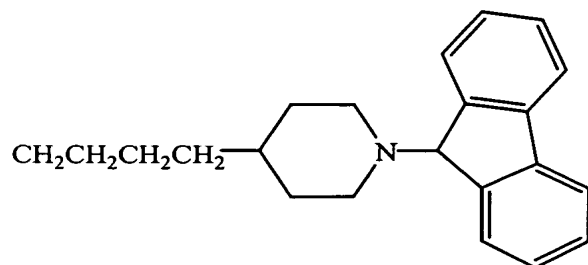
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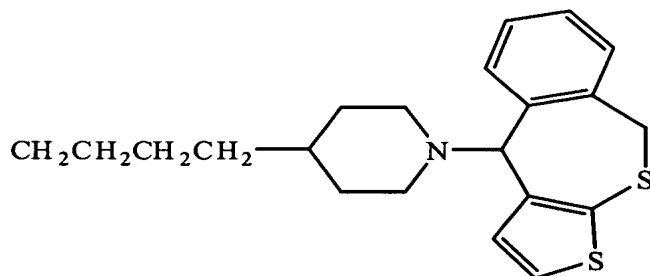
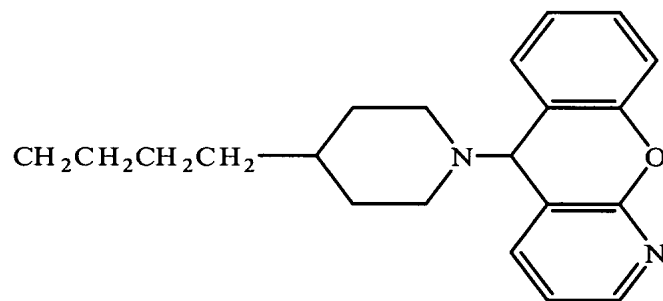
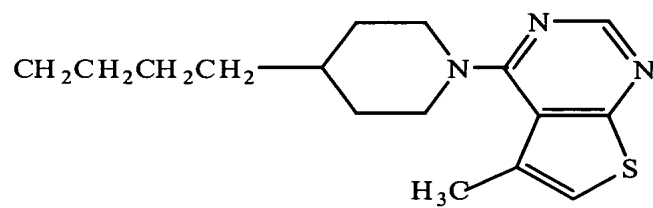
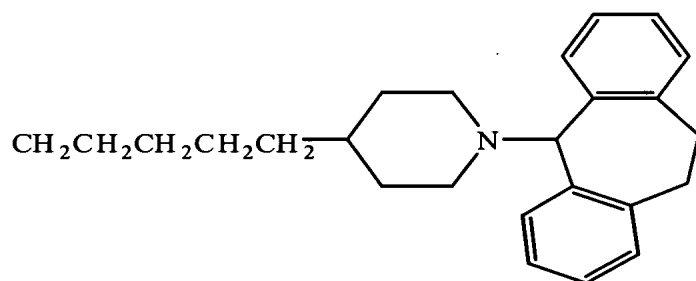
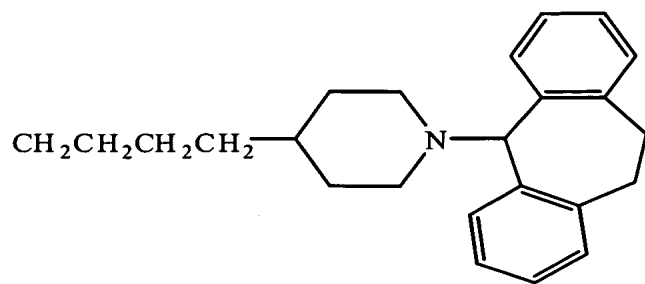
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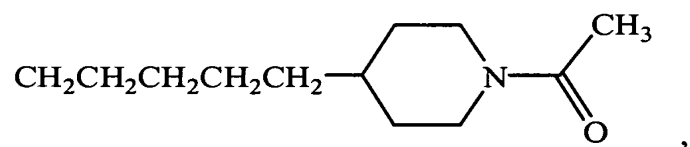
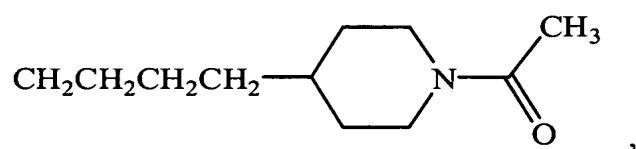
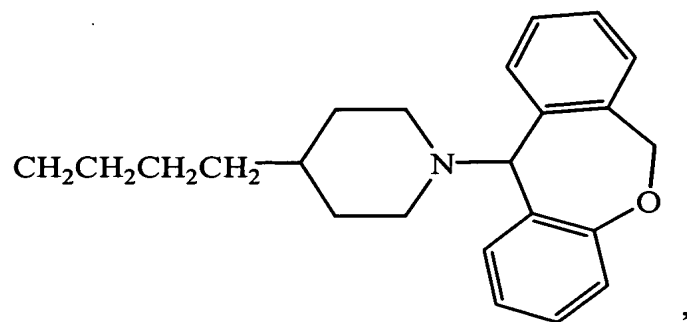


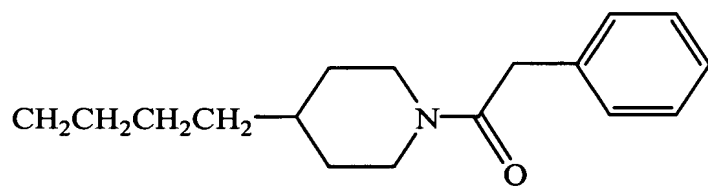
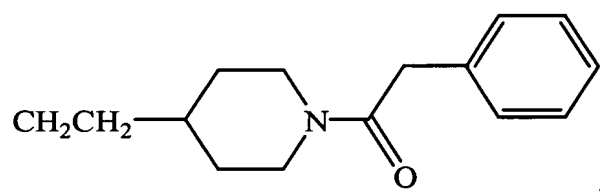
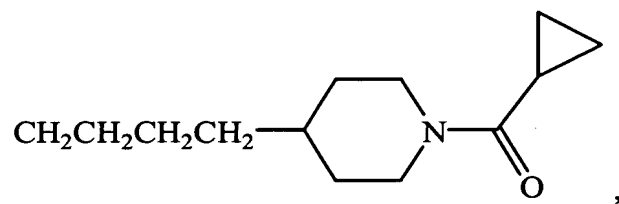
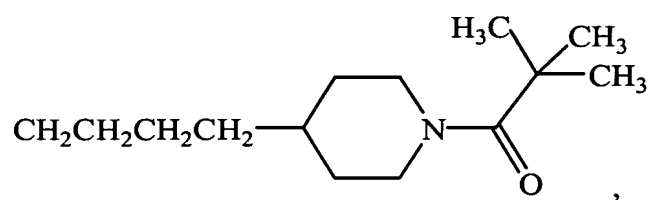
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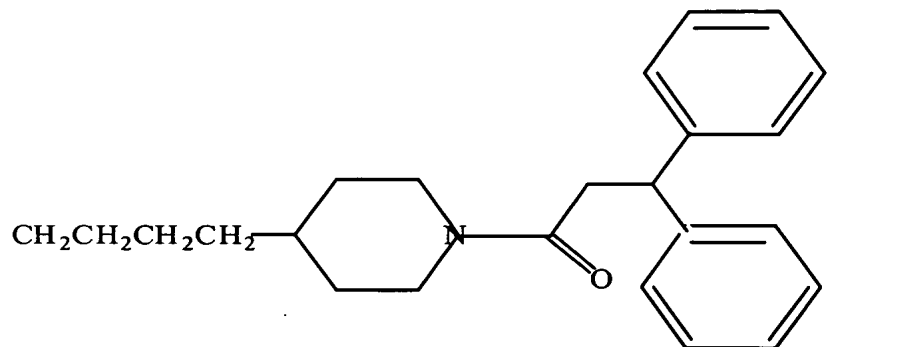
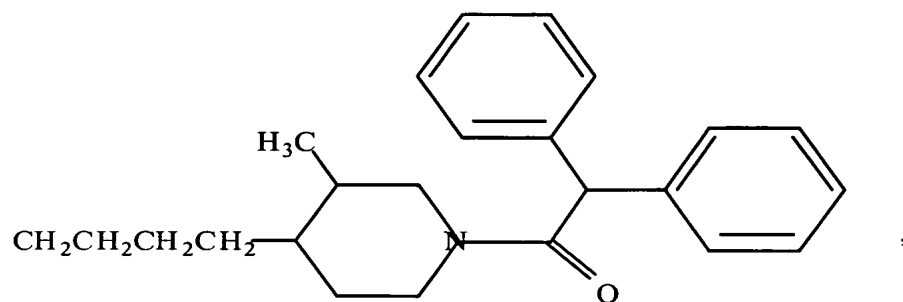
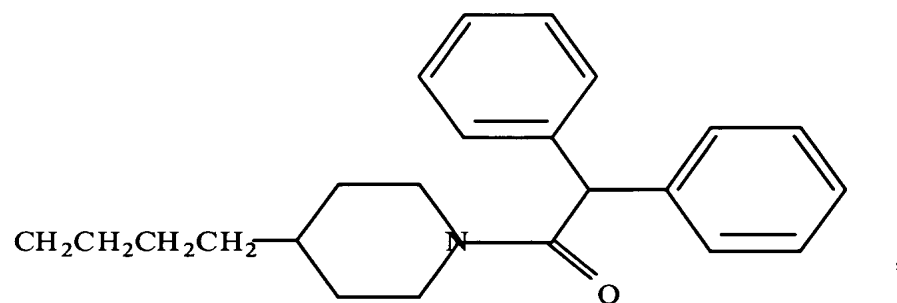
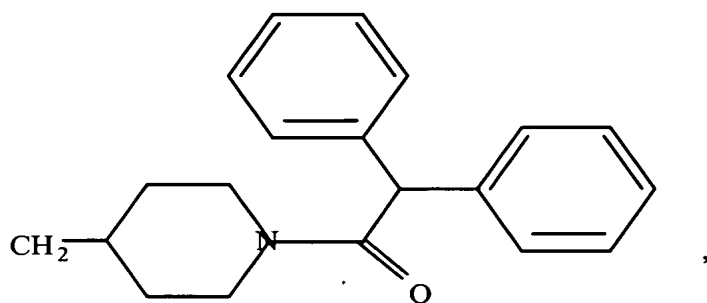


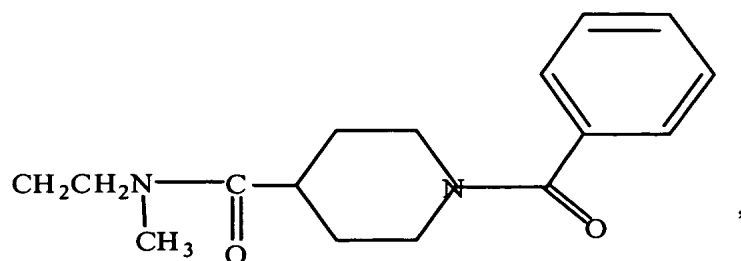
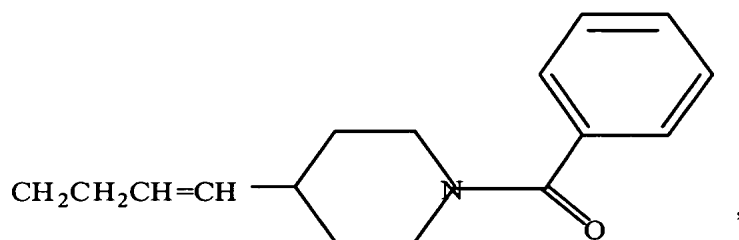
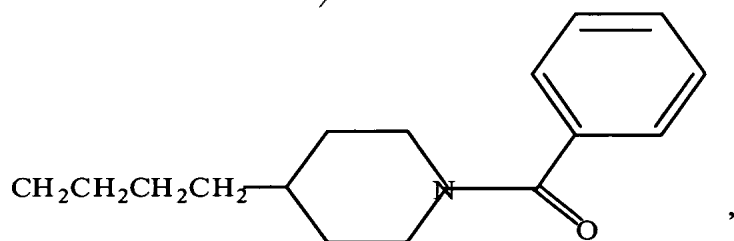
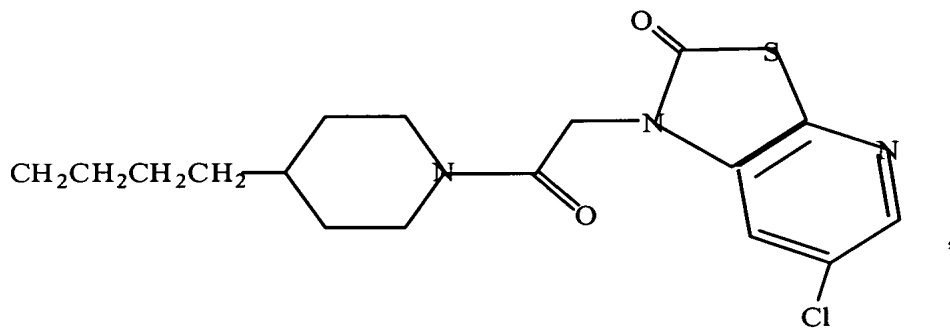
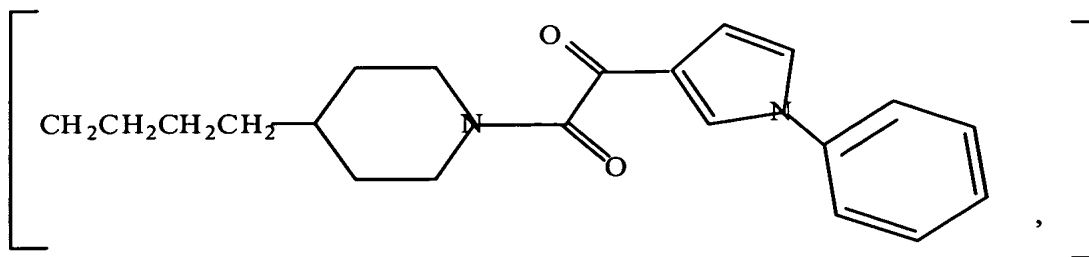
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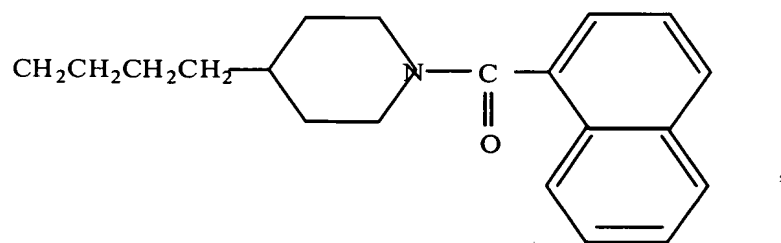
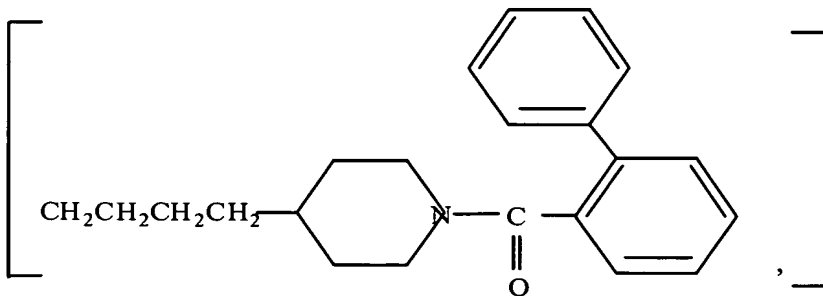
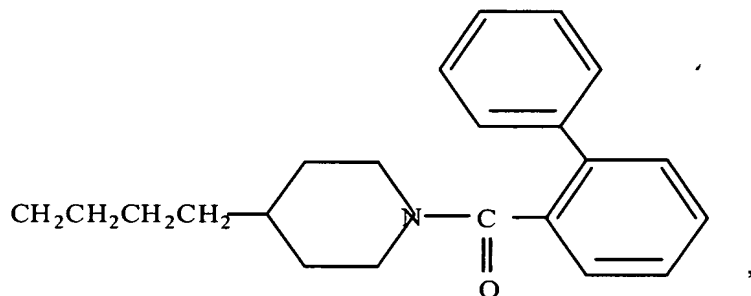
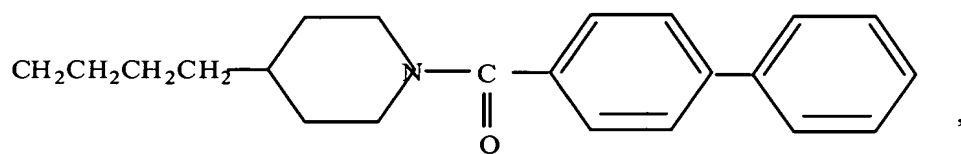
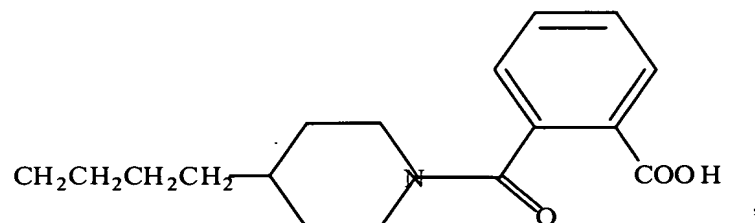
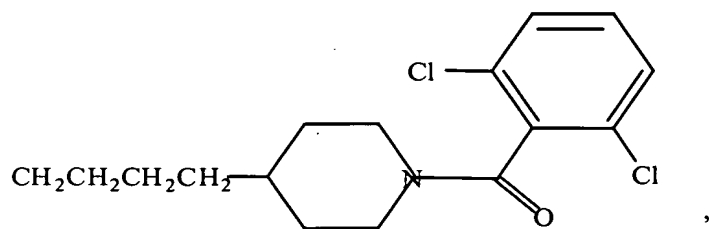


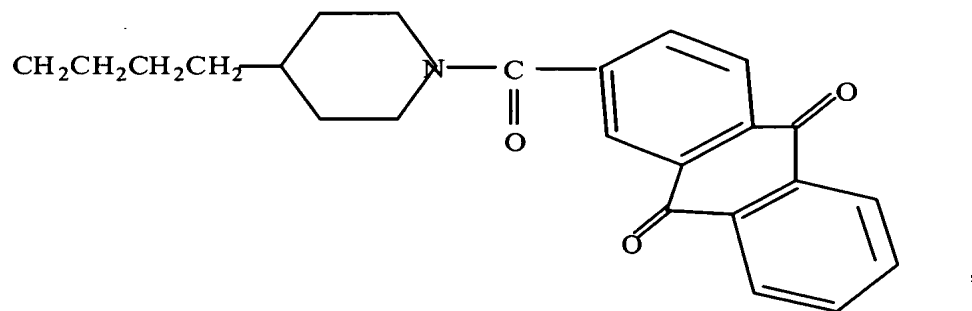
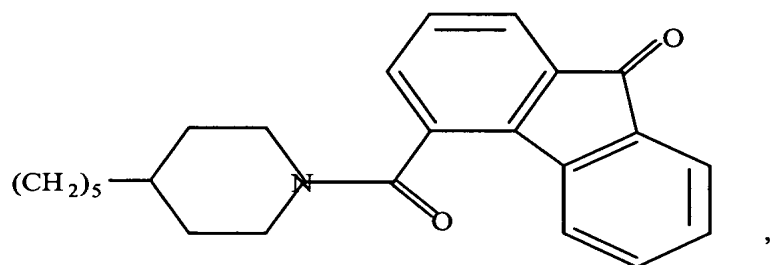
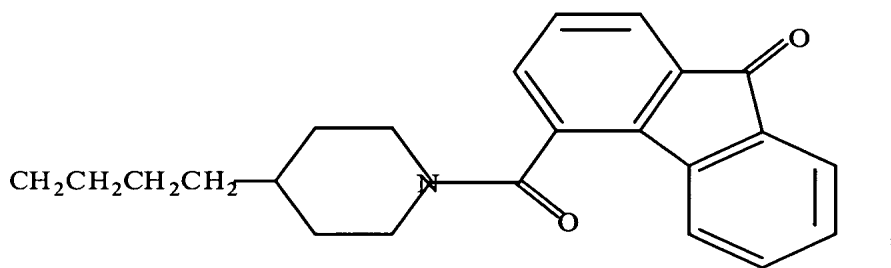
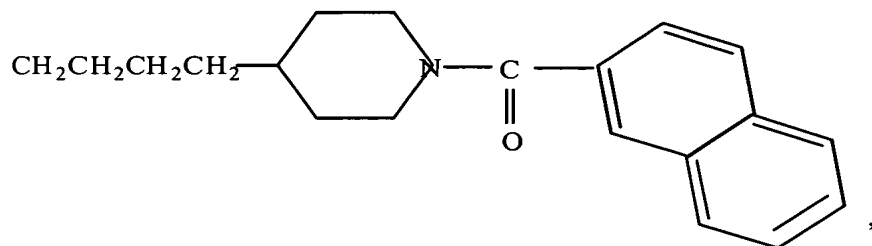
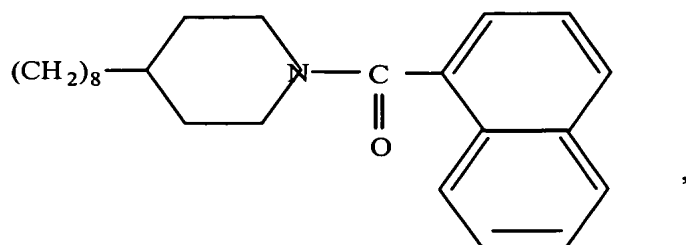


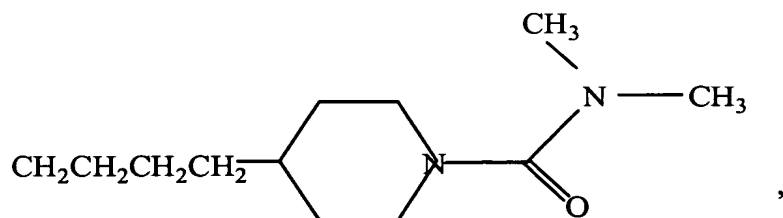
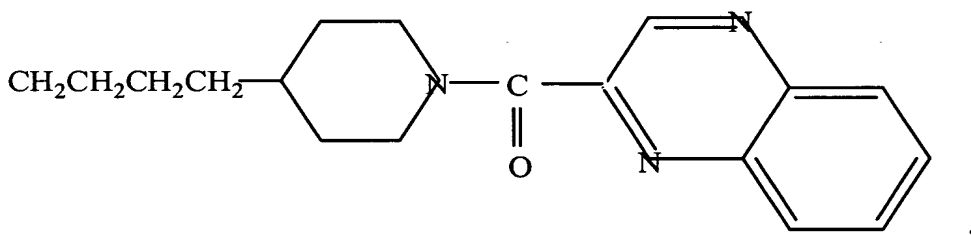
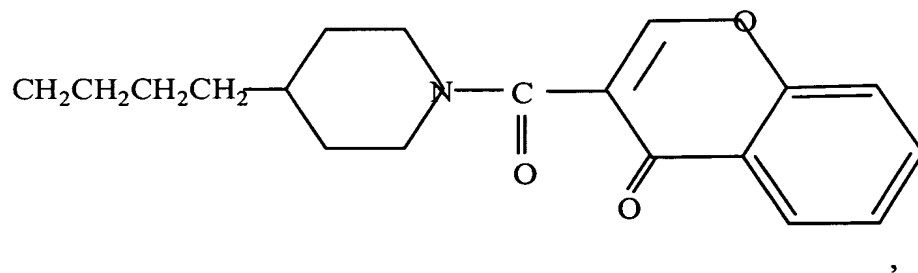
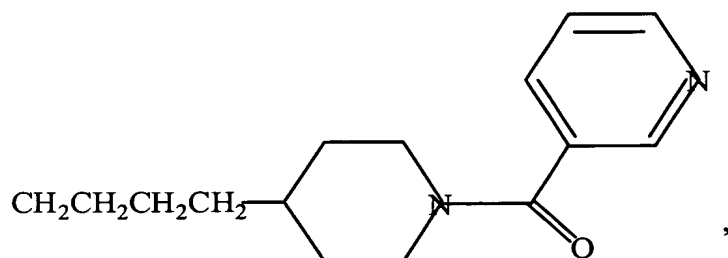
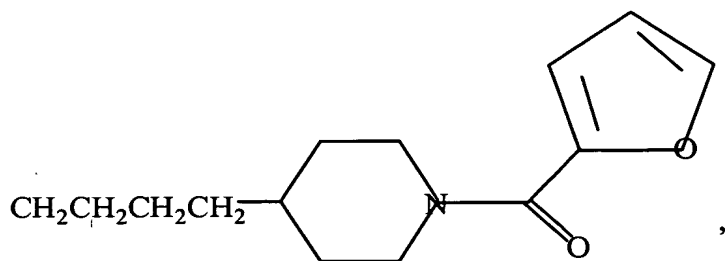


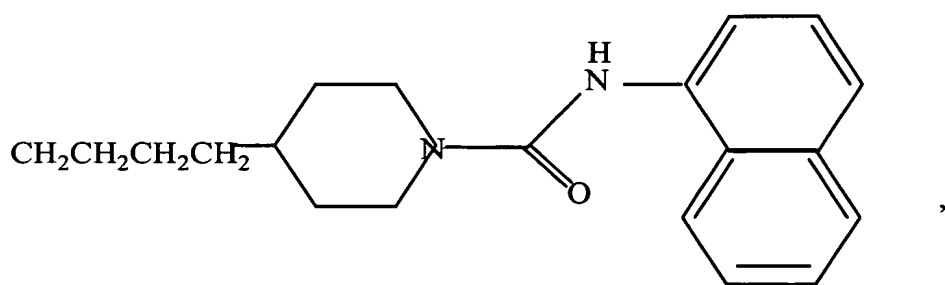
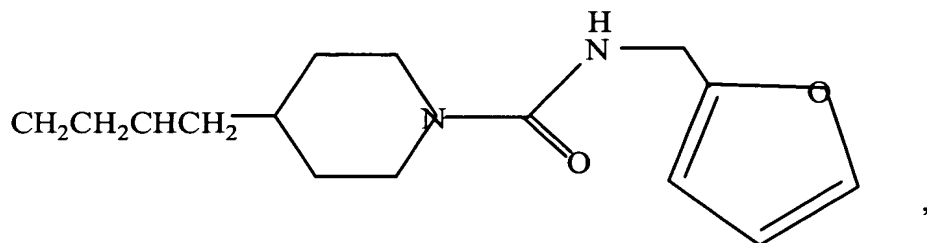
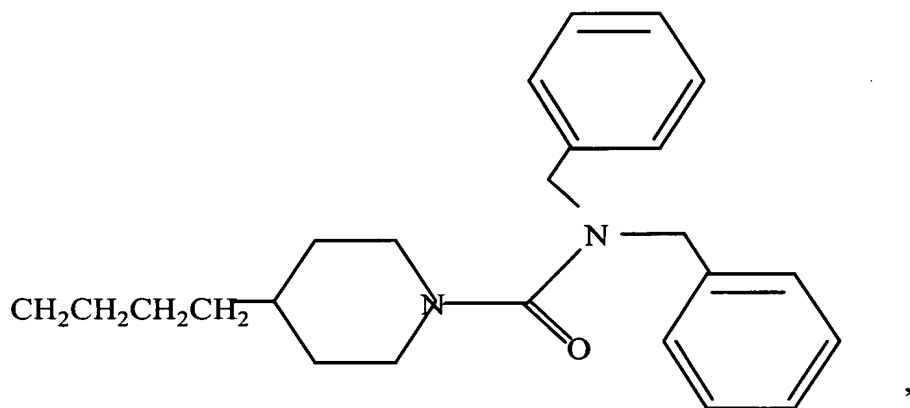
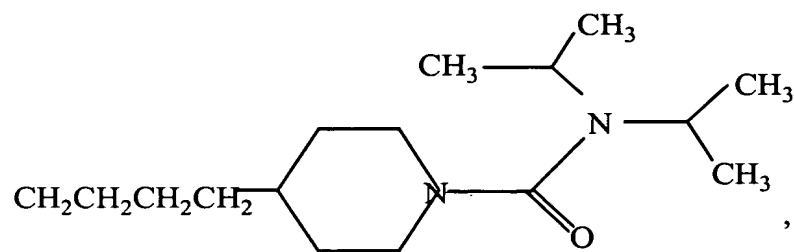


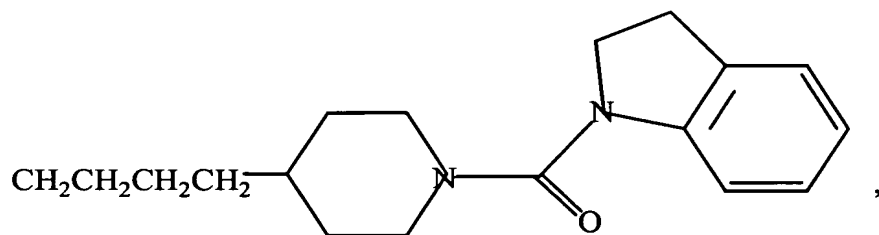
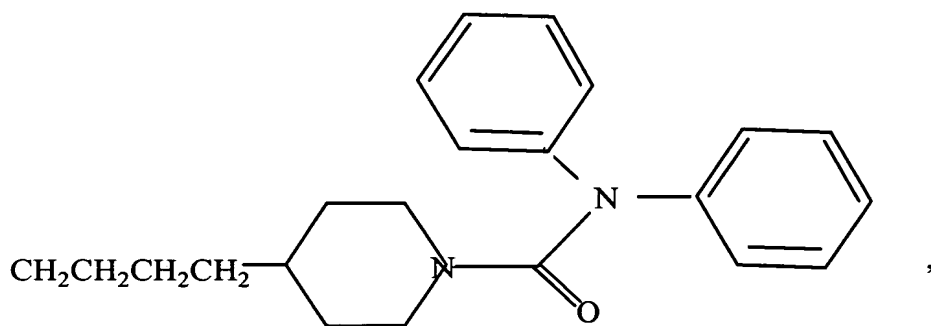
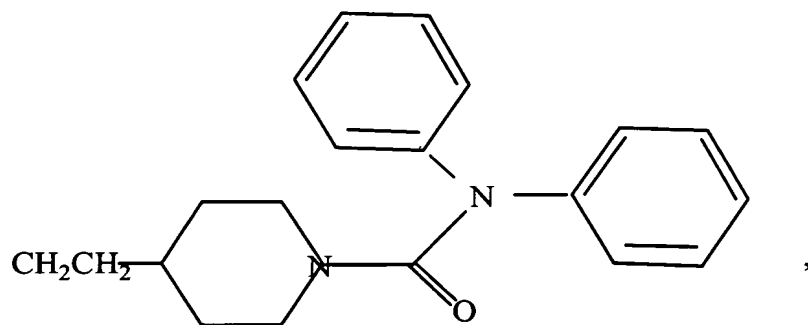
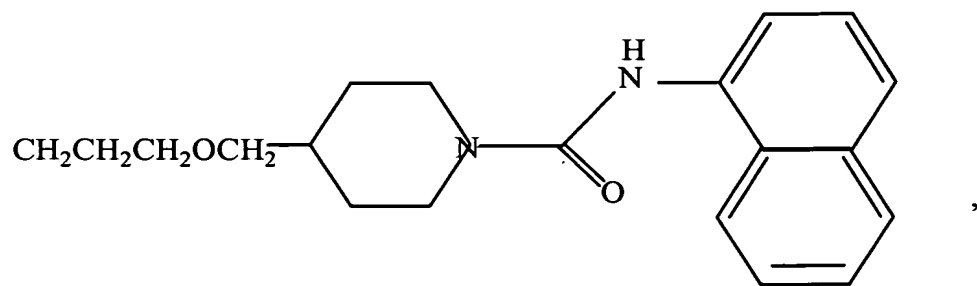


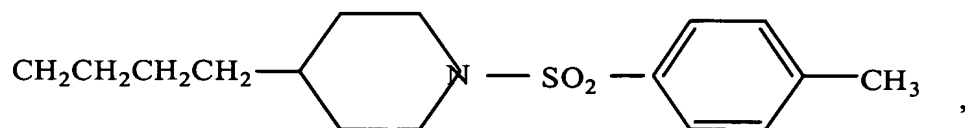
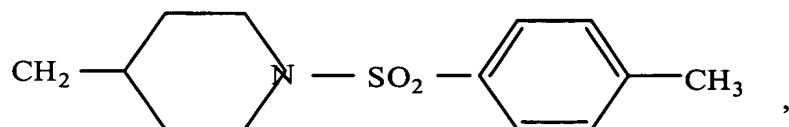
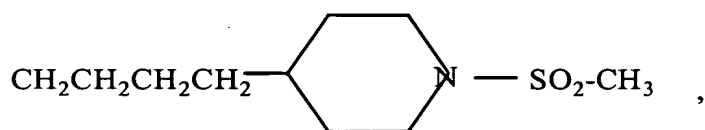
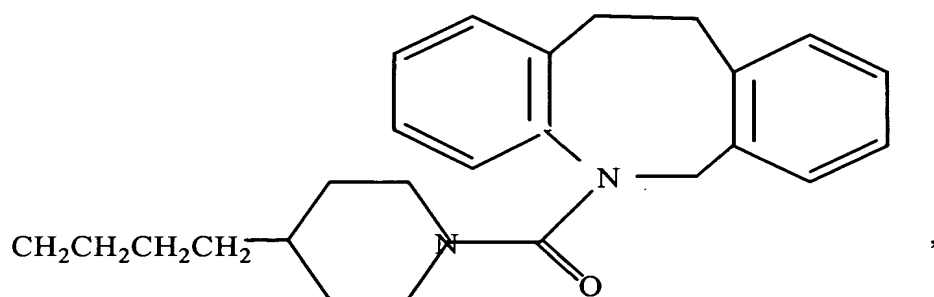
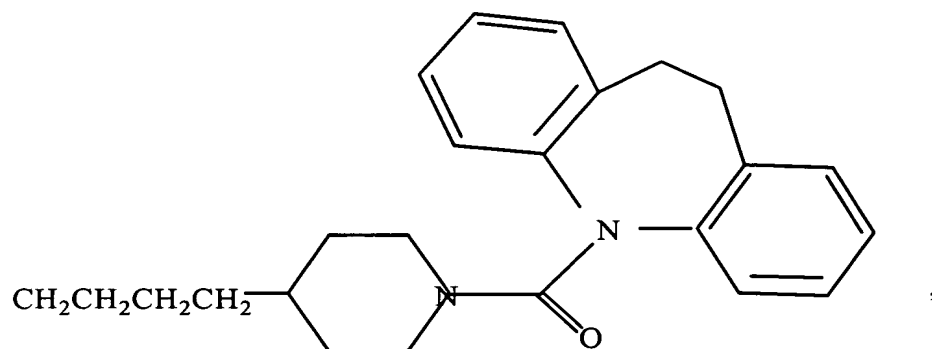


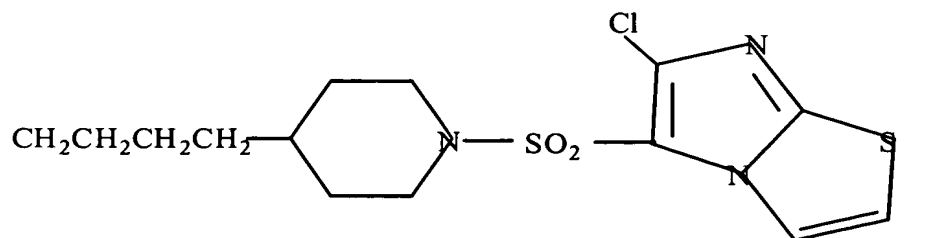
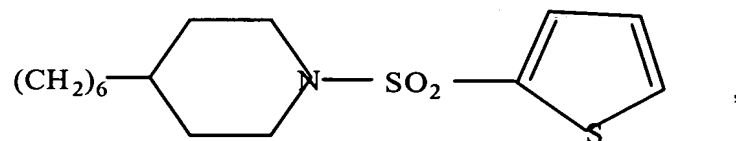
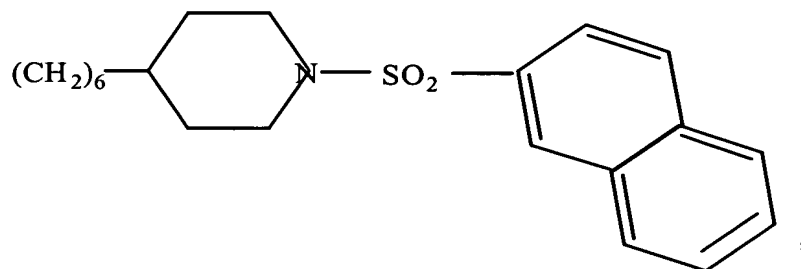
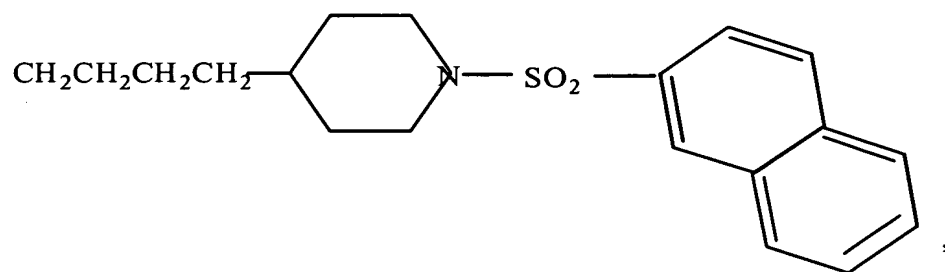
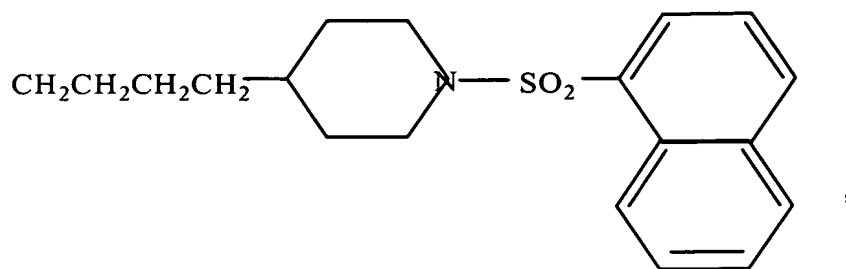


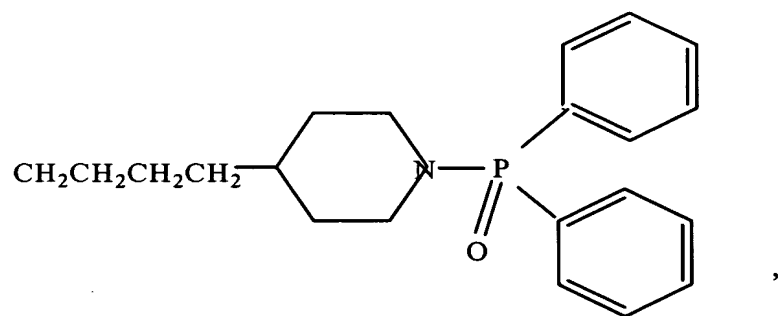
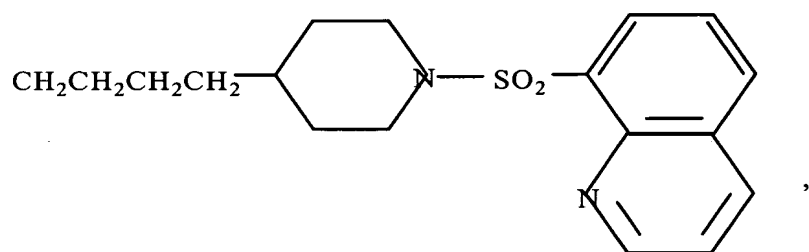
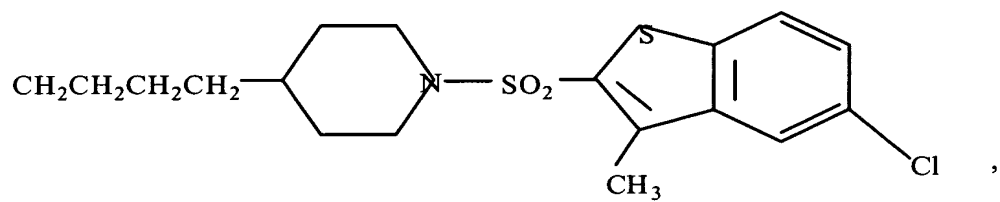
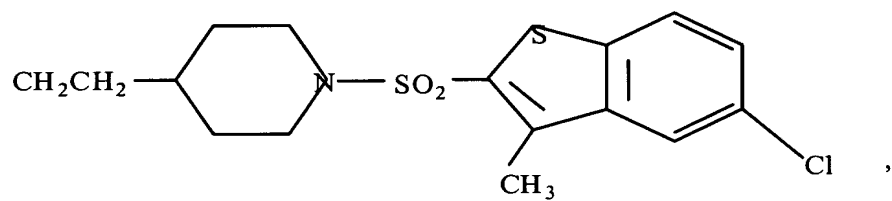
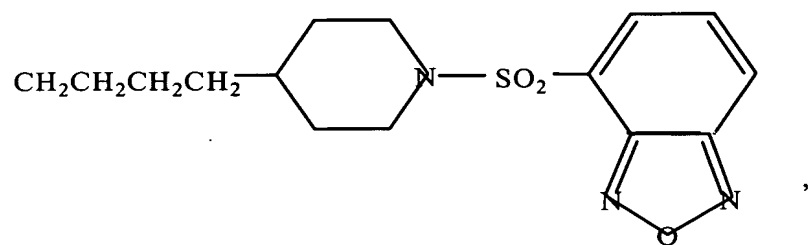


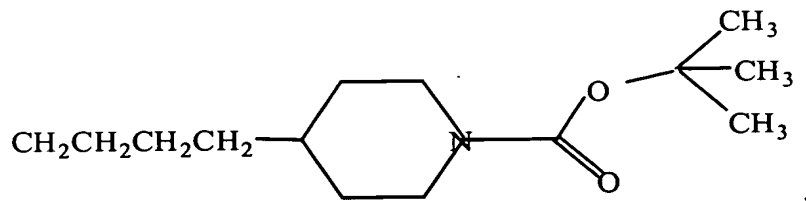
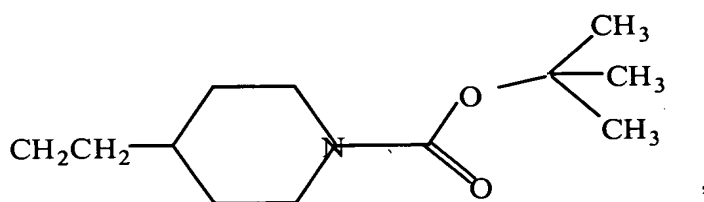
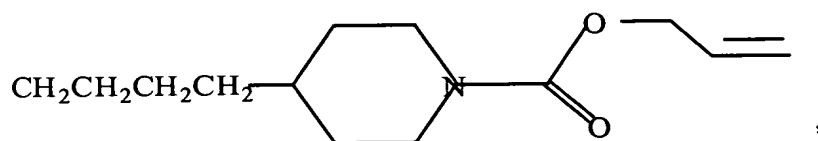
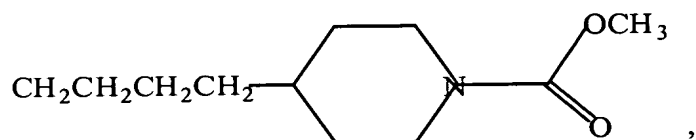
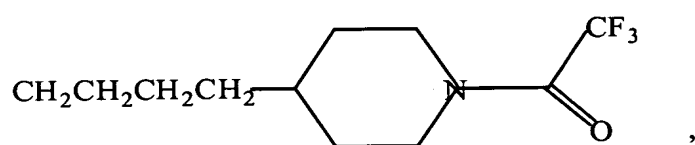
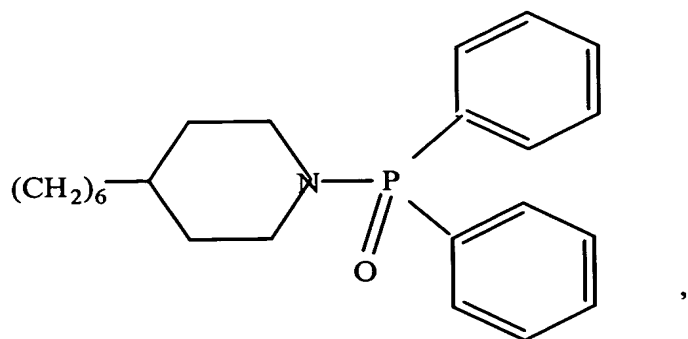


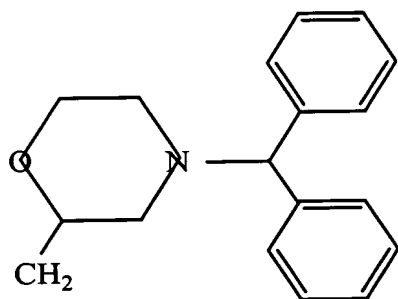
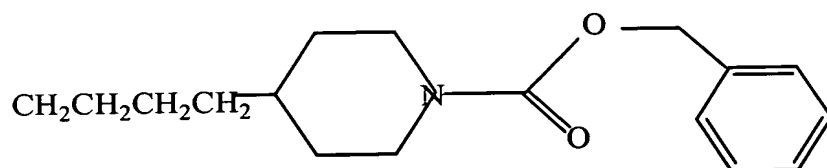
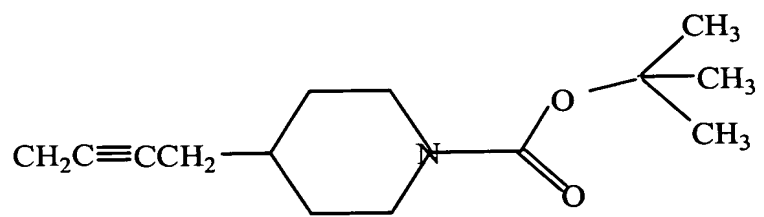
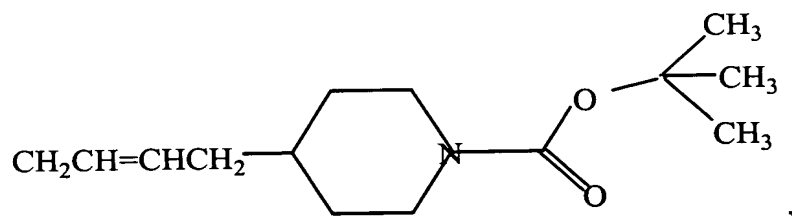
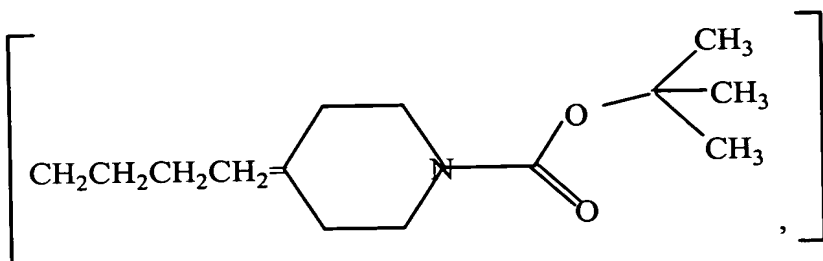


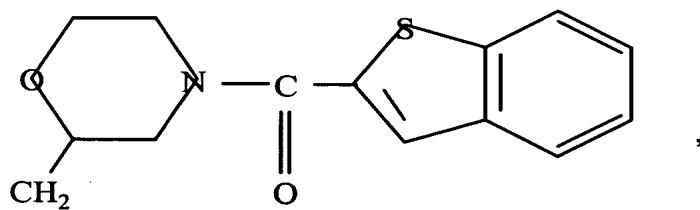
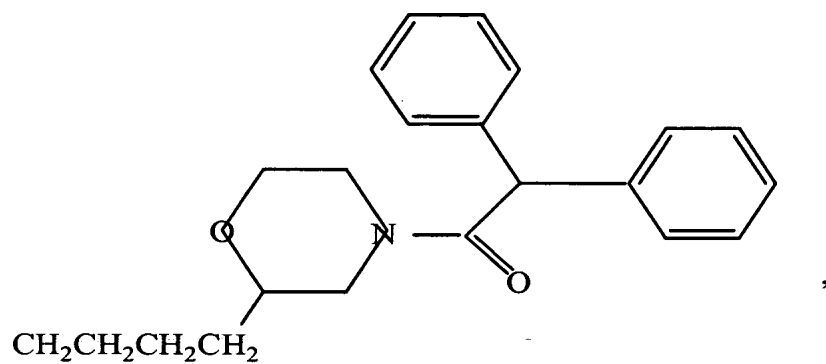
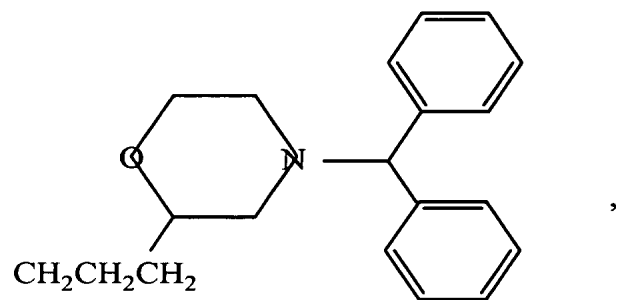
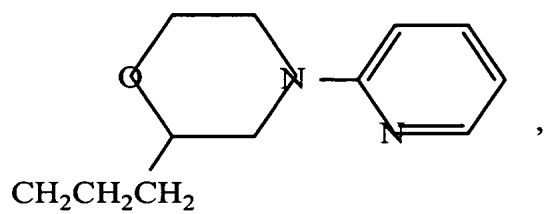


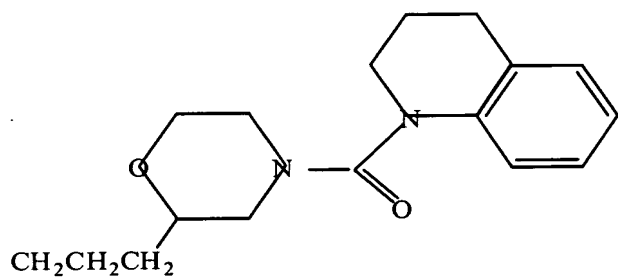




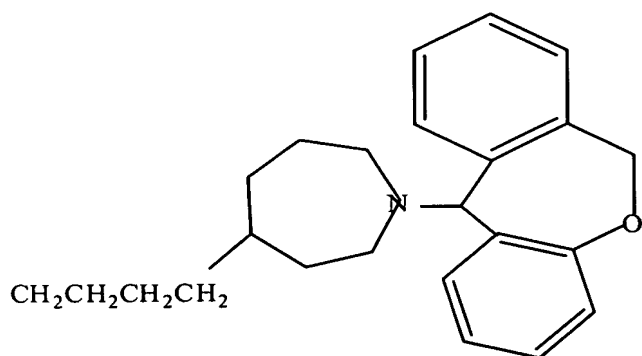
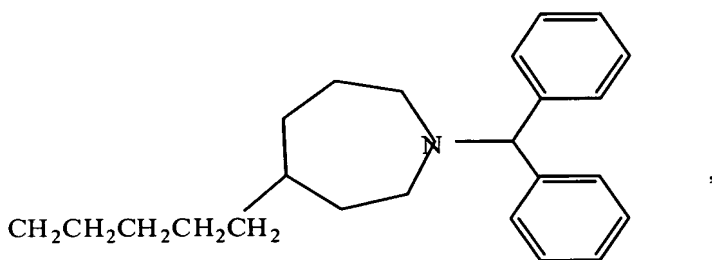
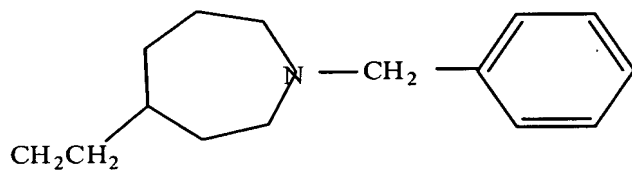
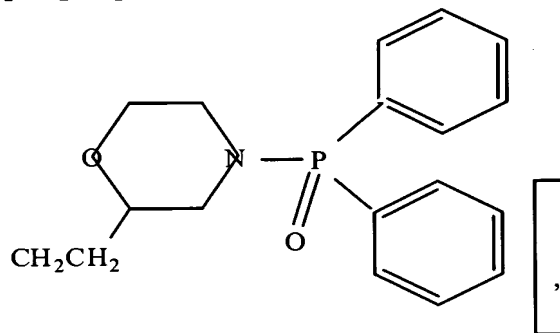


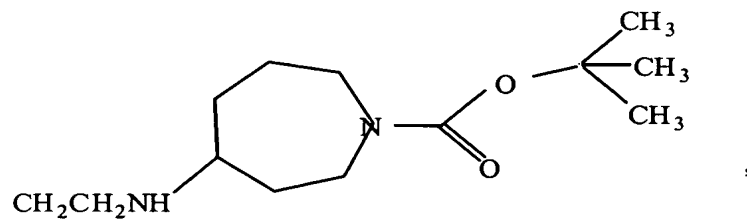
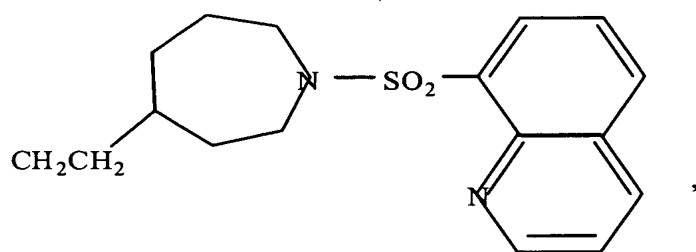
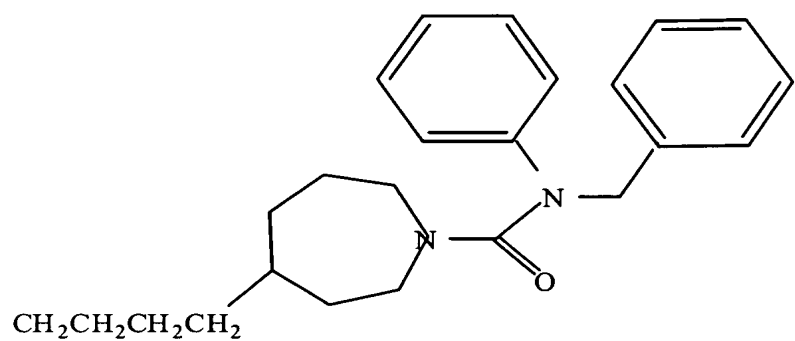
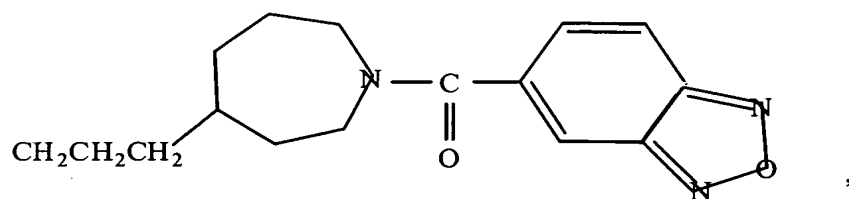
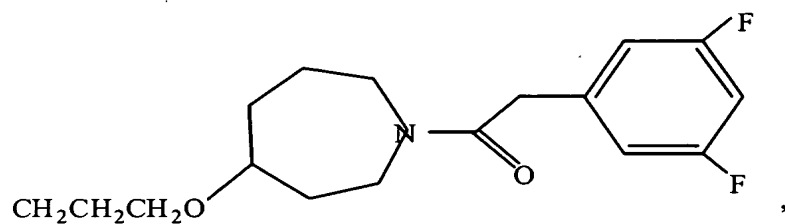


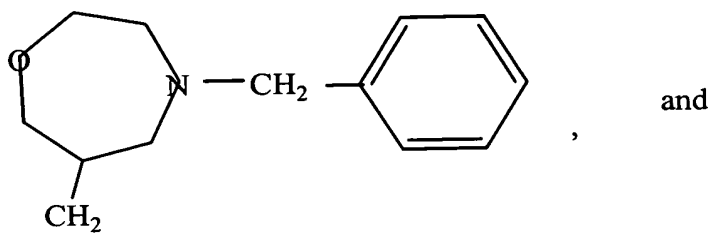
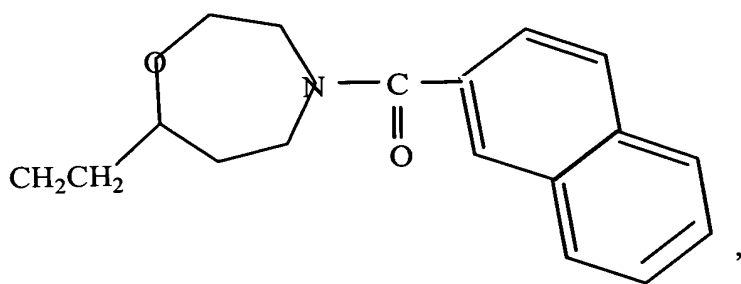
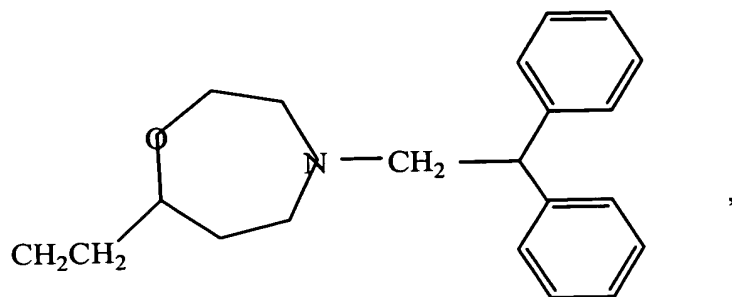




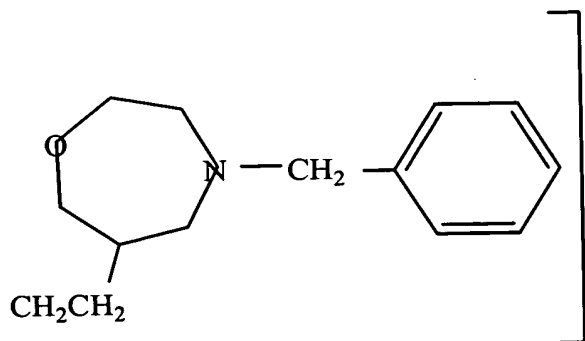
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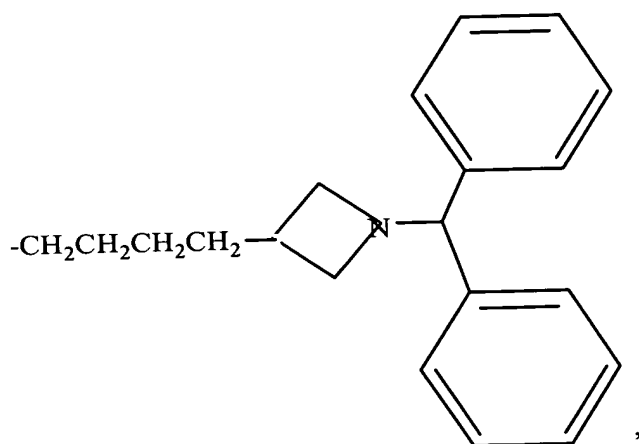
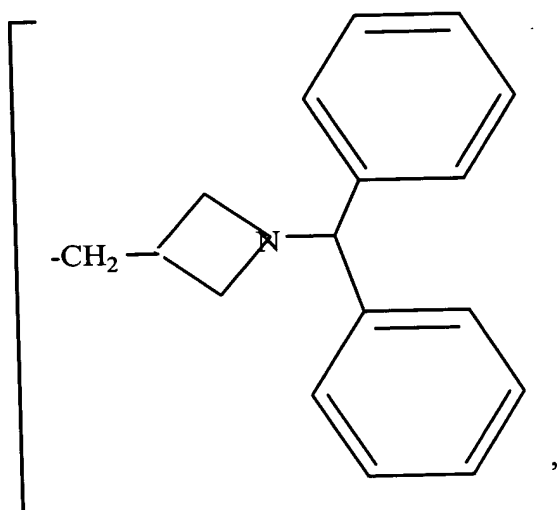


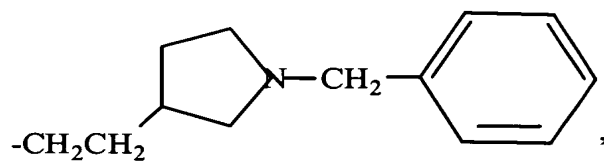
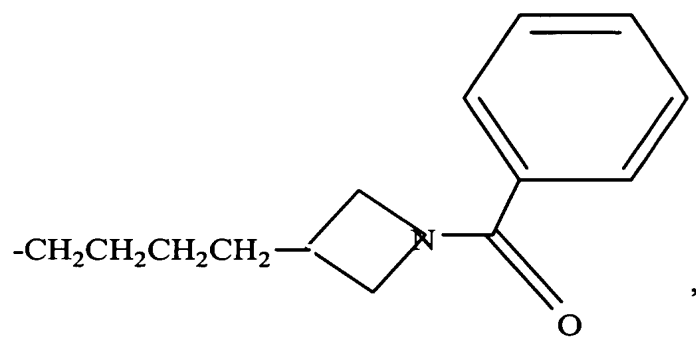
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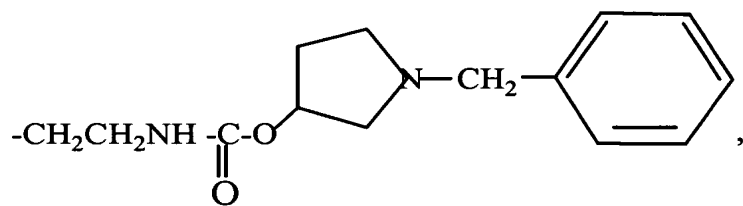
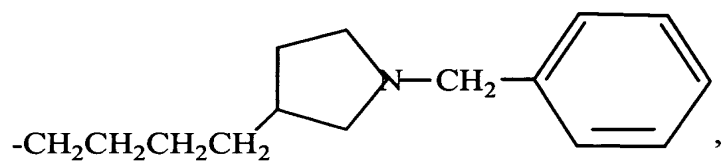
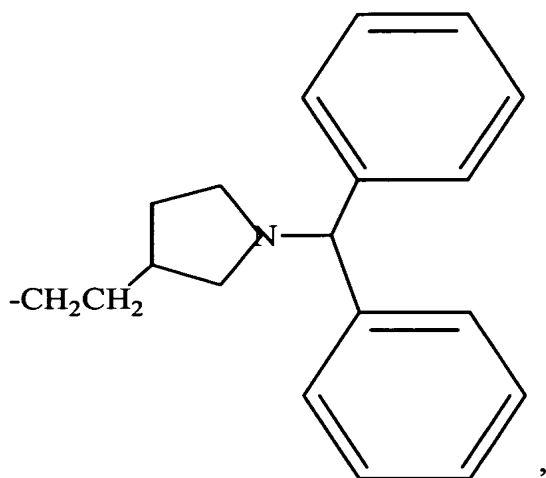


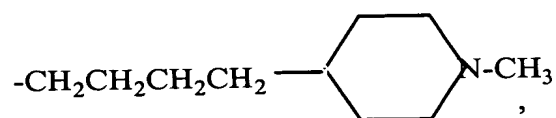
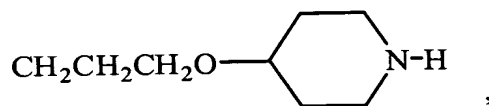
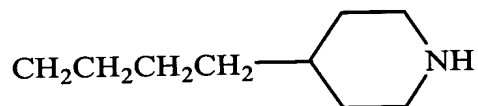
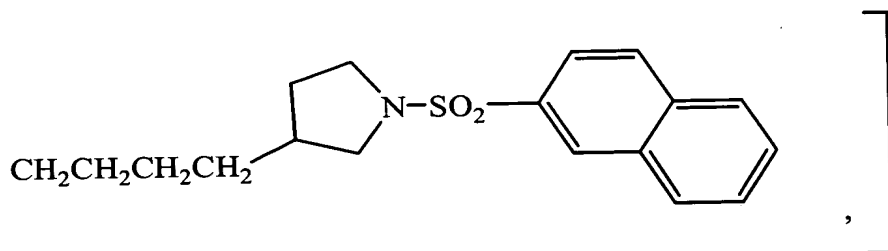
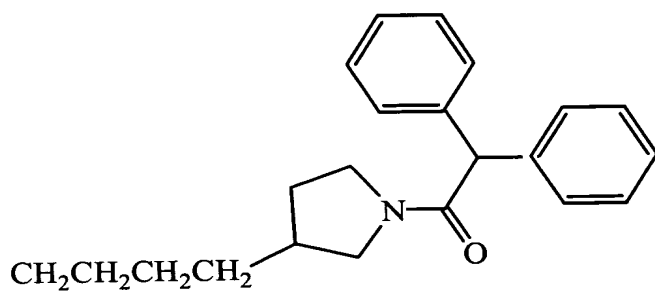
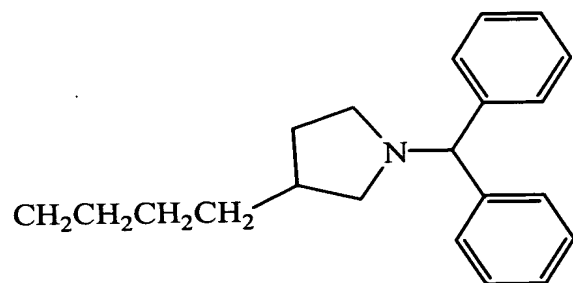
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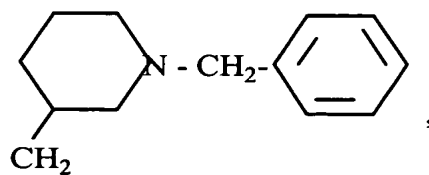
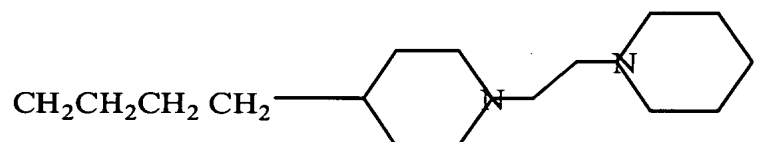
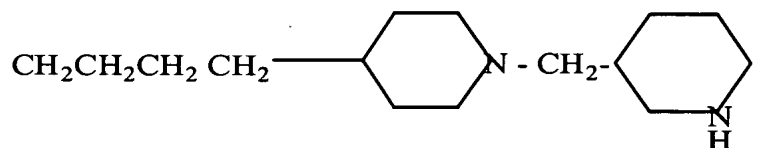
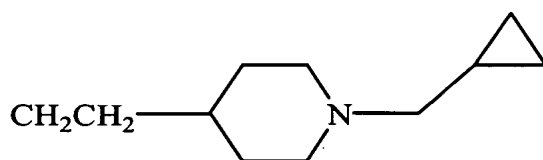
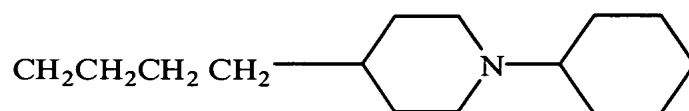
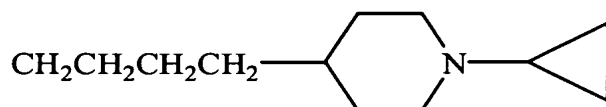
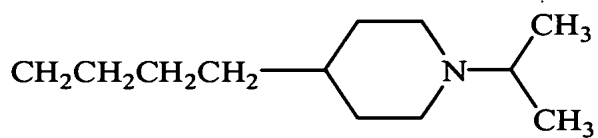
77. A method of inhibiting tumor cell growth according to claim 64, wherein DEG is selected from the group consisting of

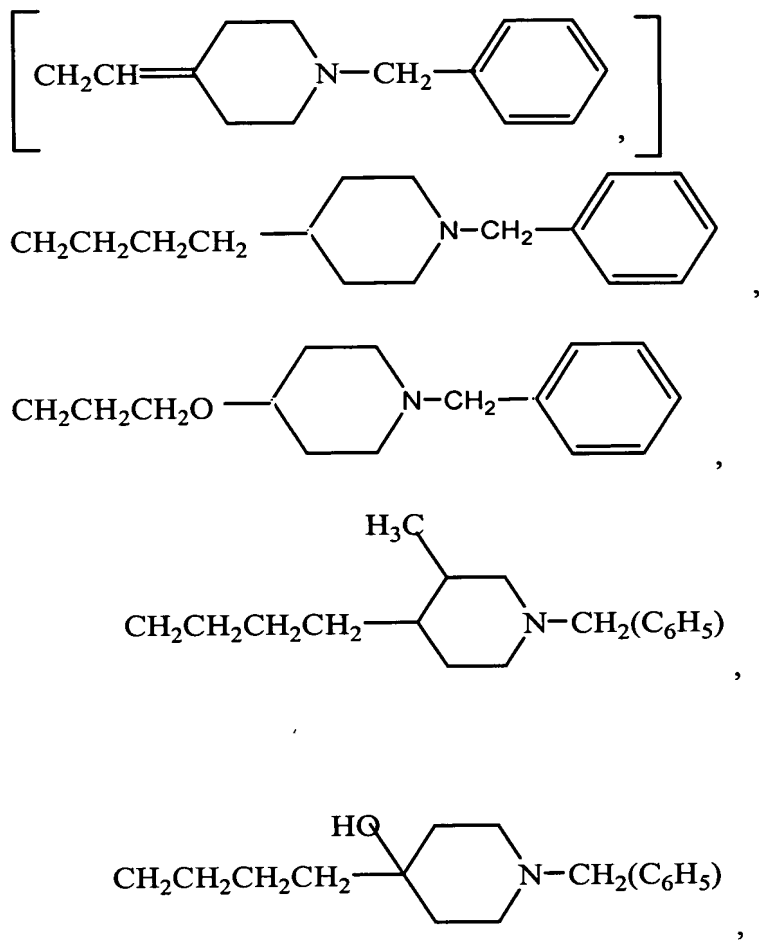


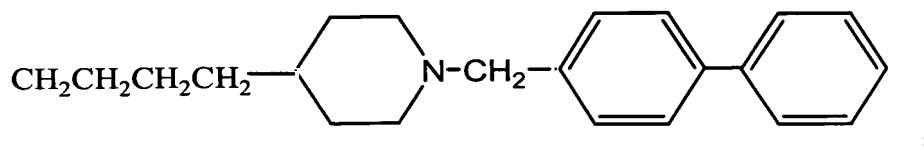
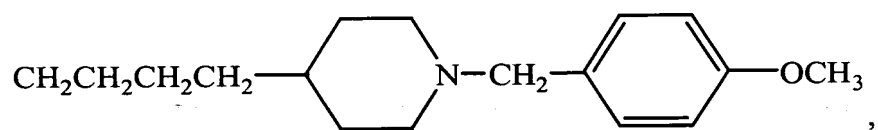
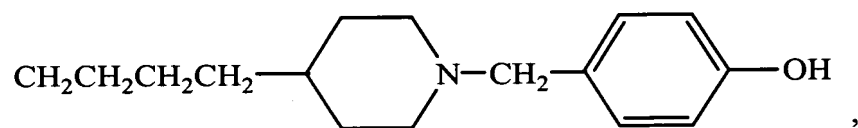
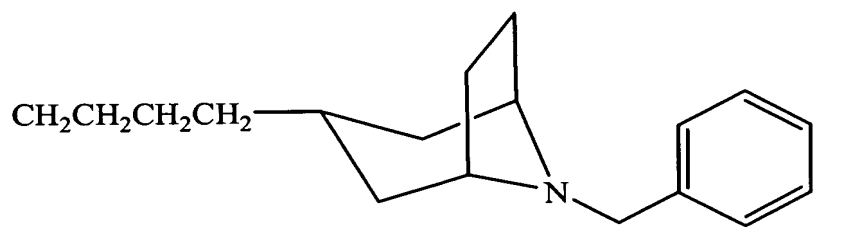
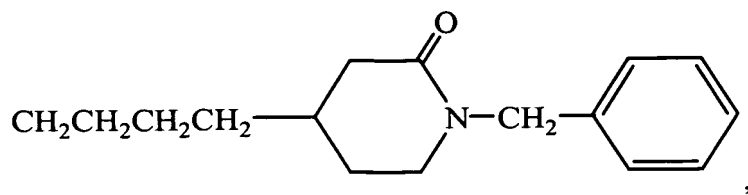


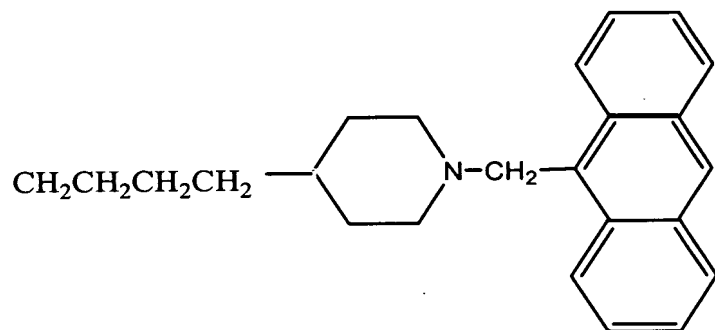




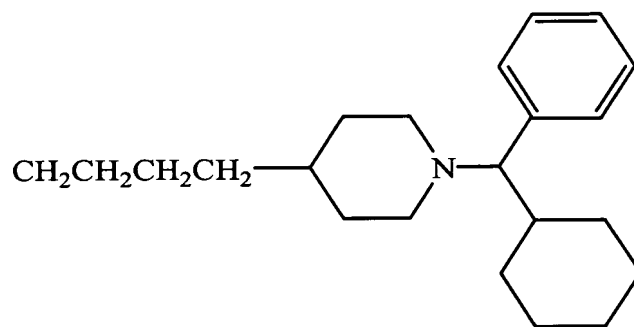




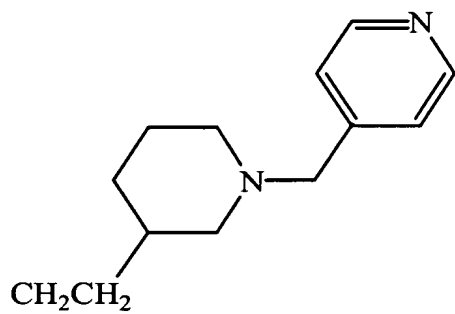




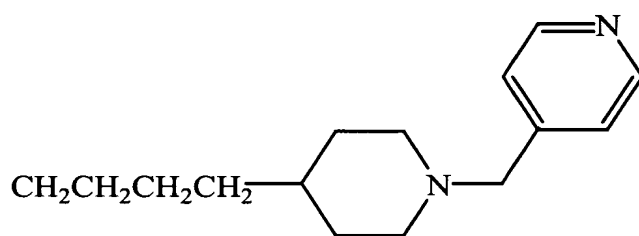
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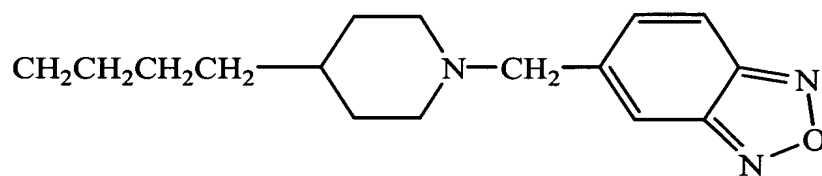
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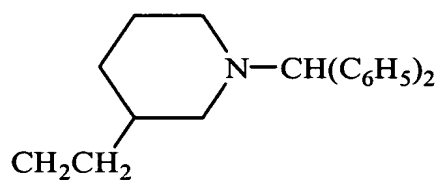
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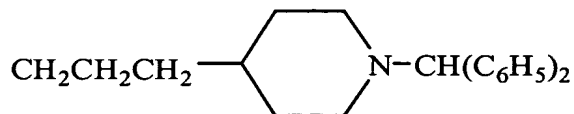
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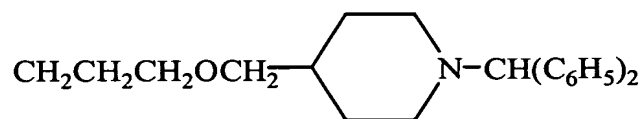
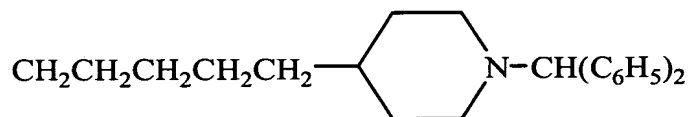
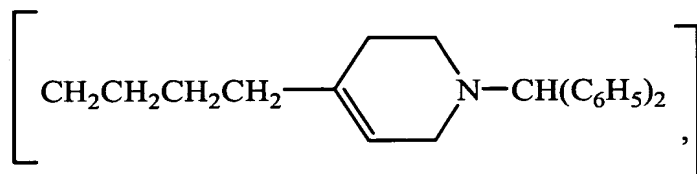
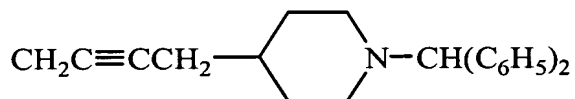
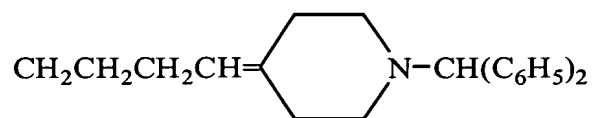
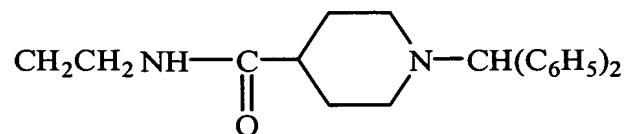
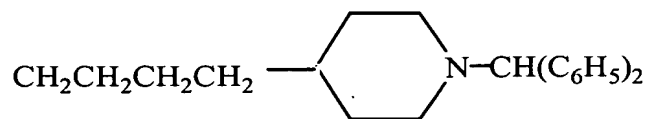
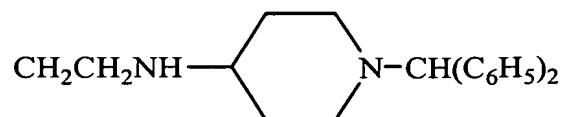
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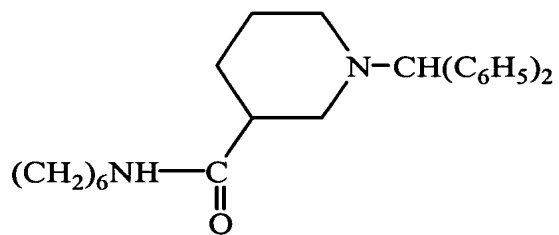
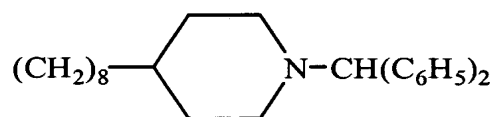
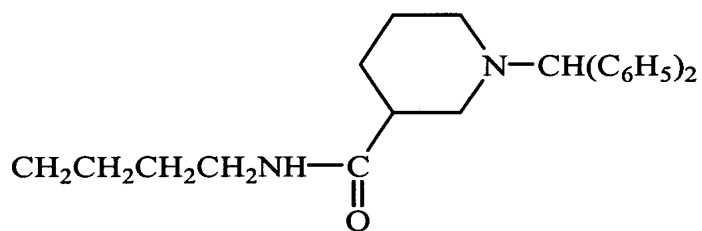
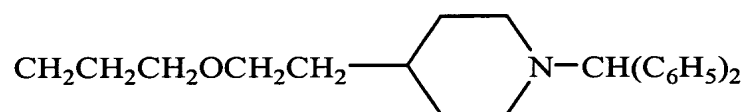
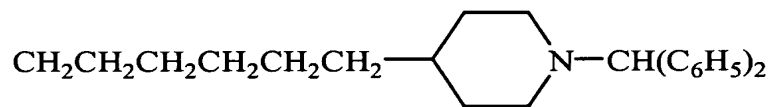
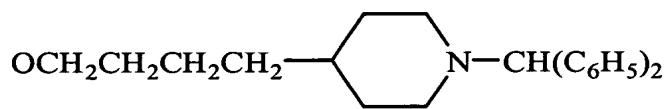


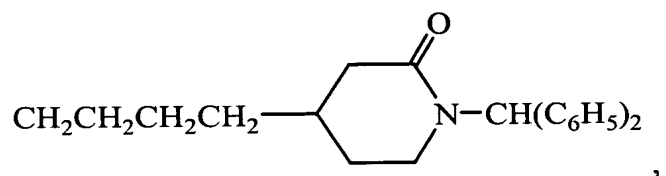
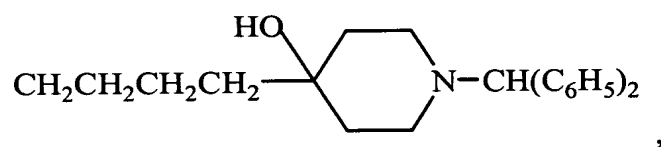
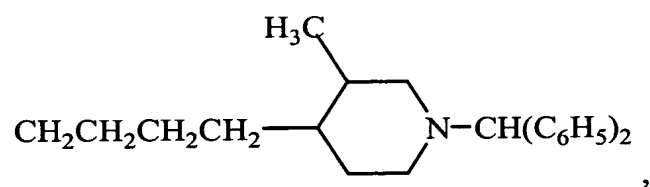
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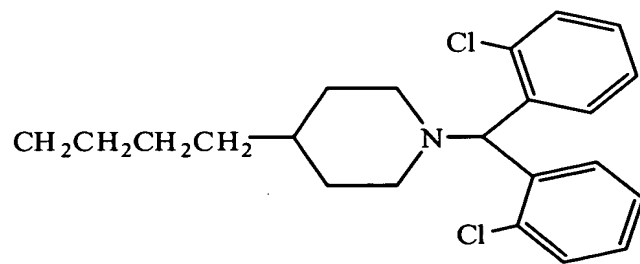
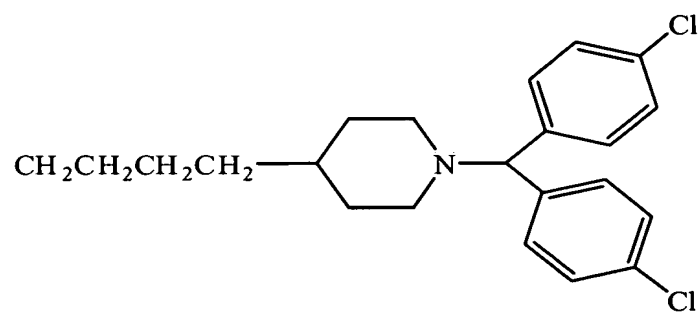
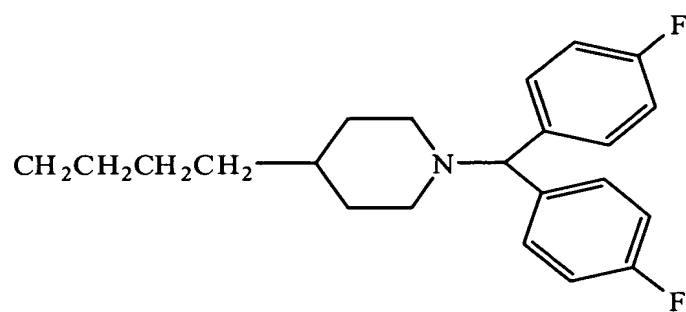
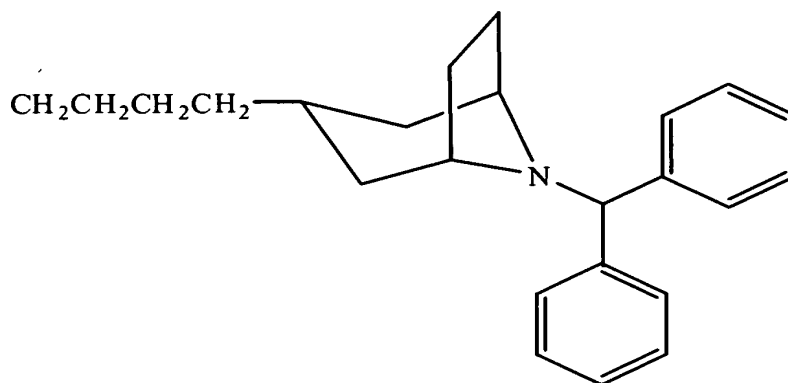


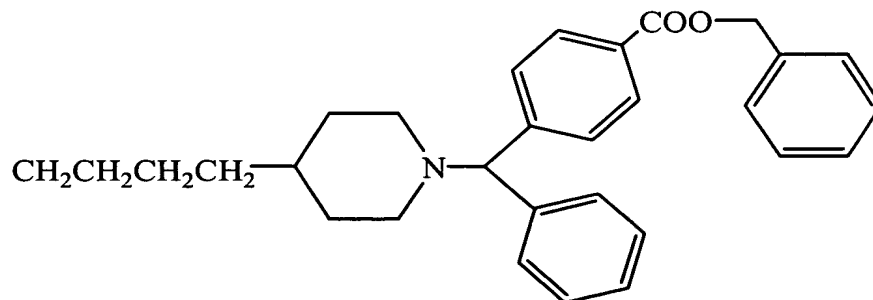
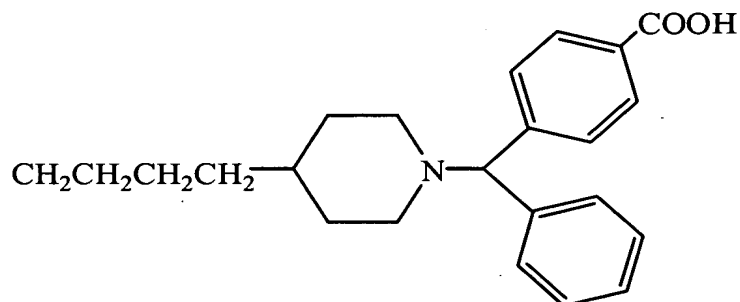
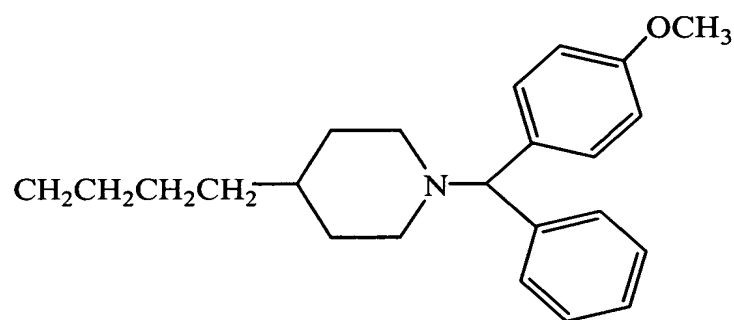
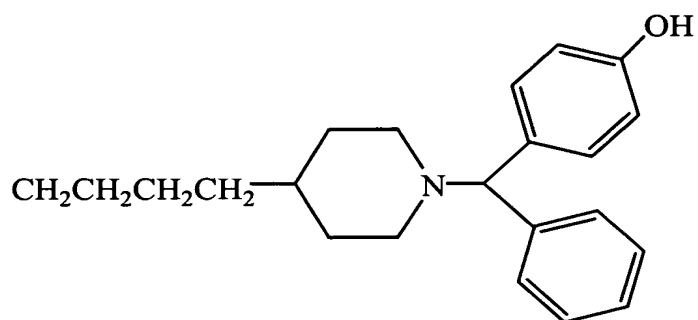
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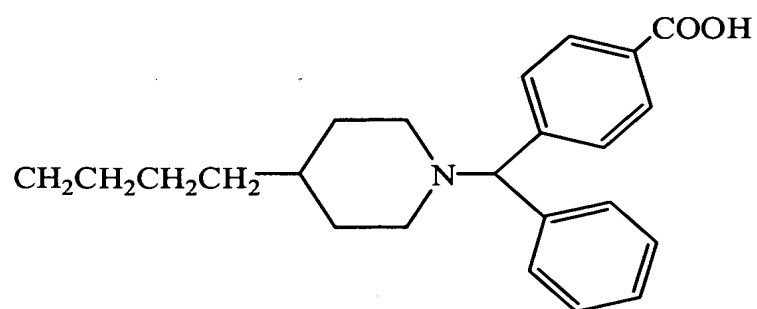
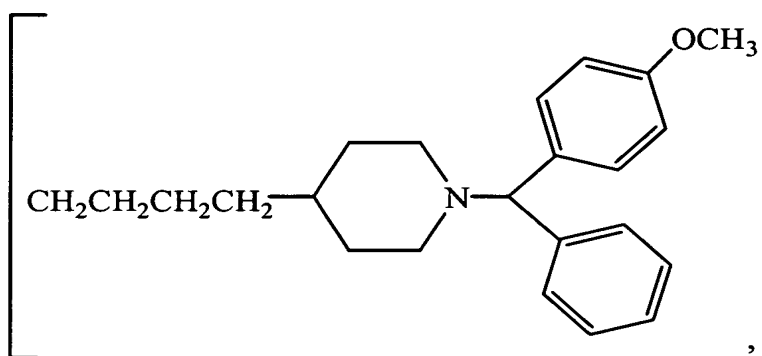
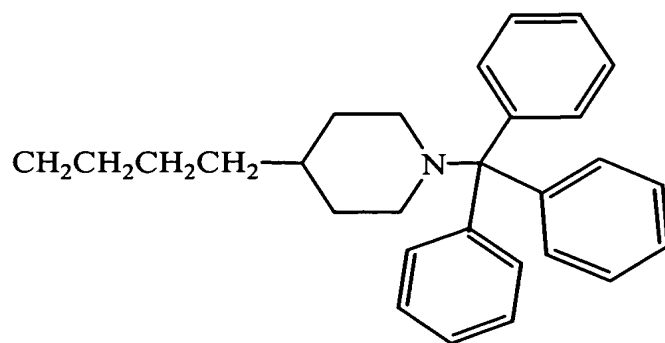


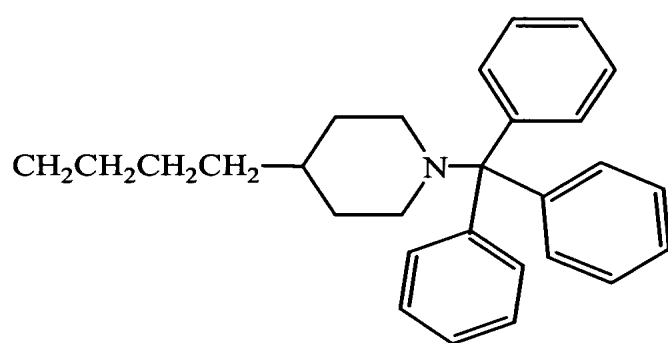
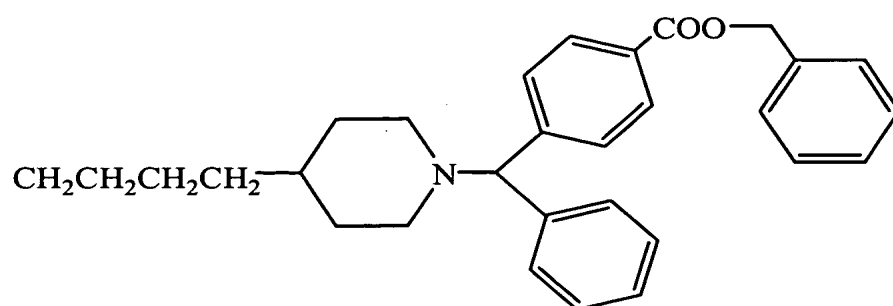


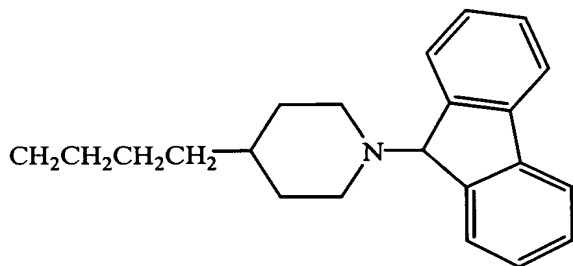
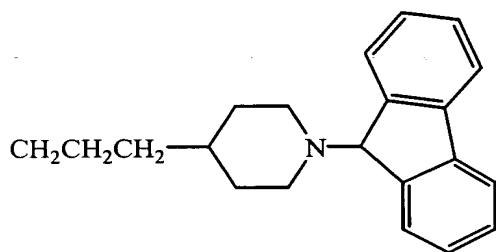
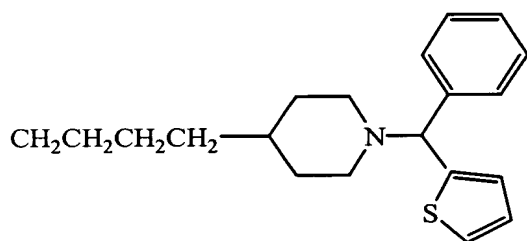
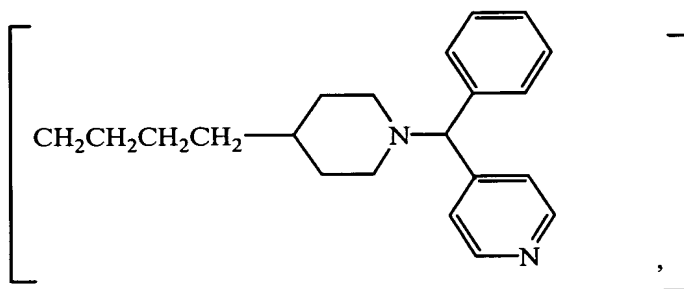
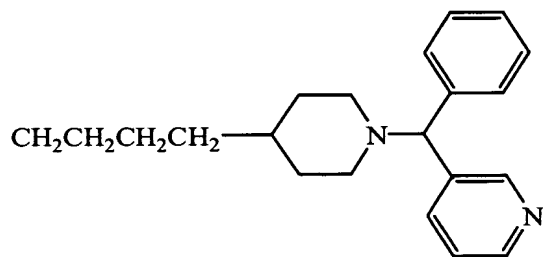


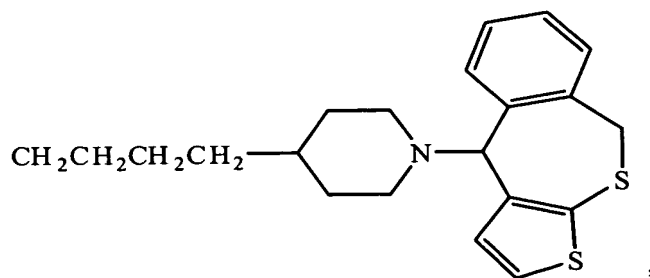
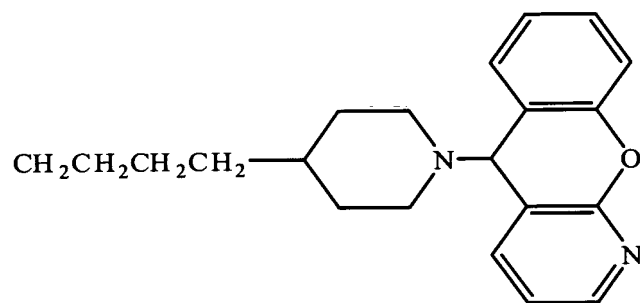
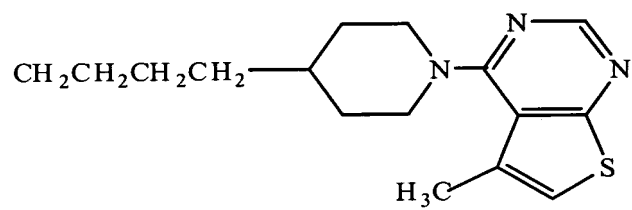
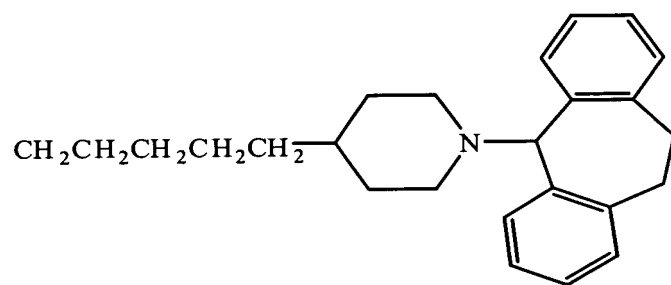
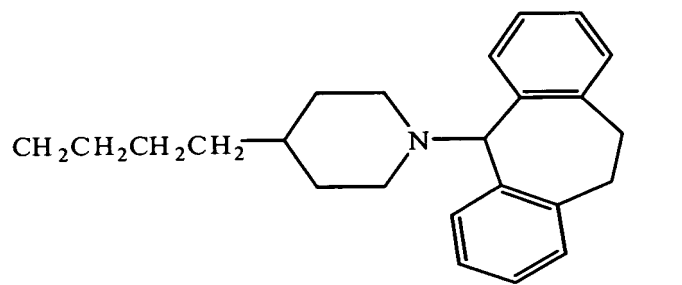


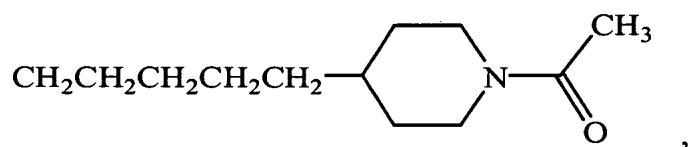
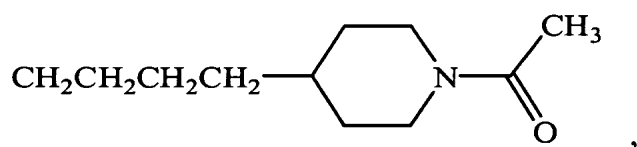
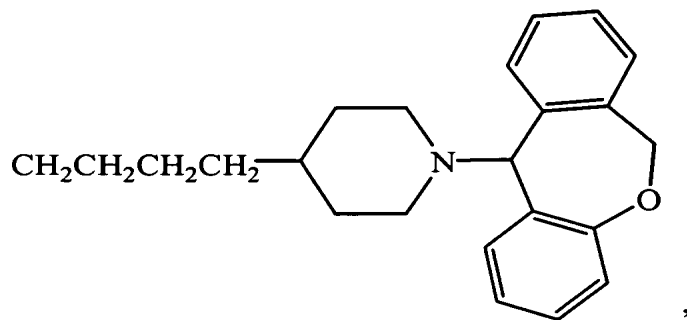


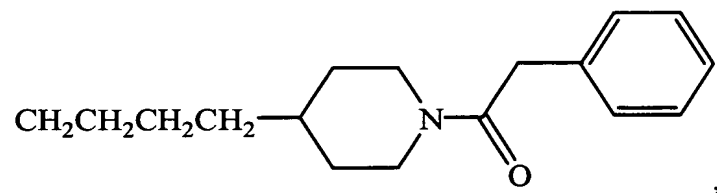
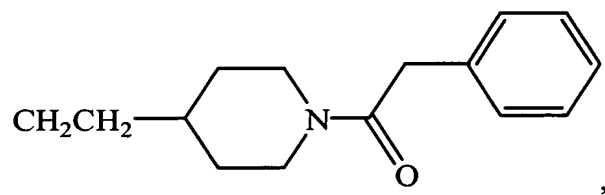
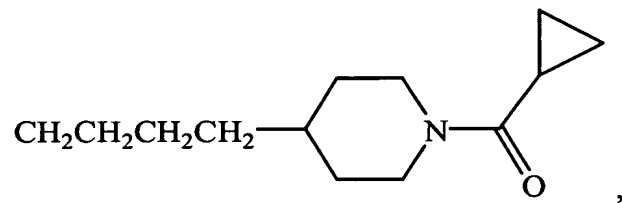
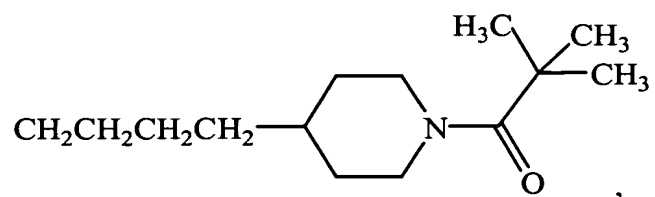


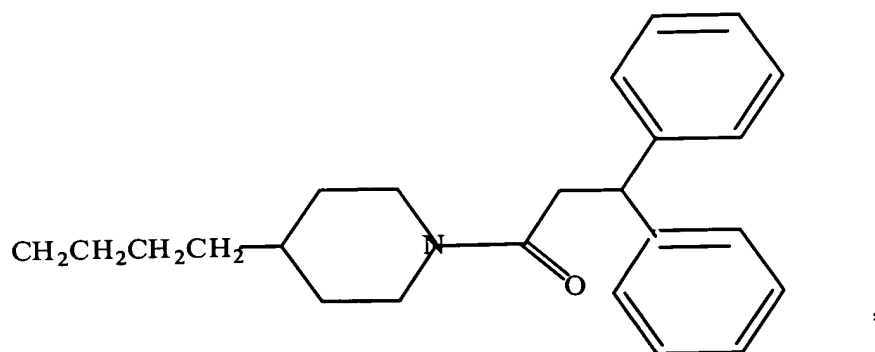
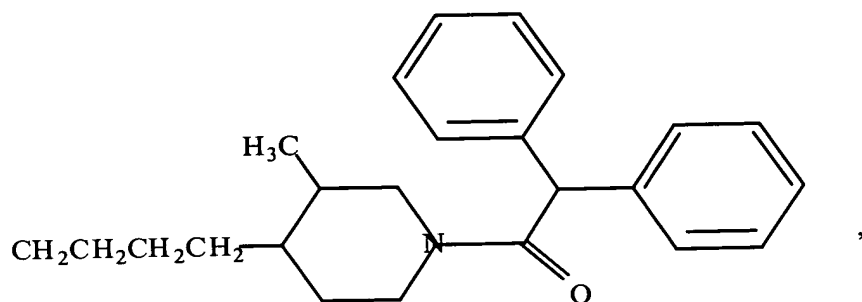
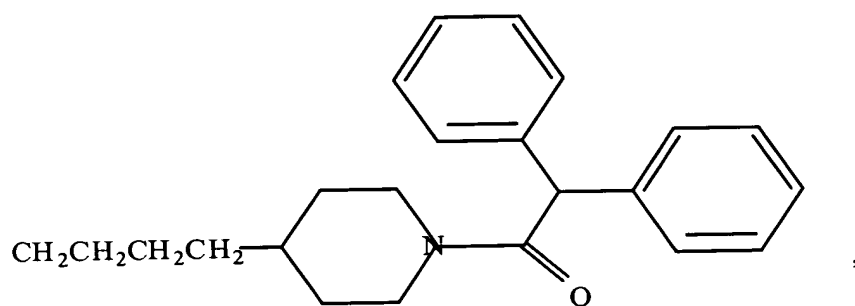
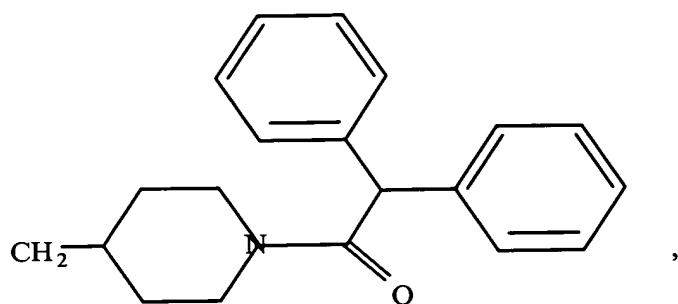


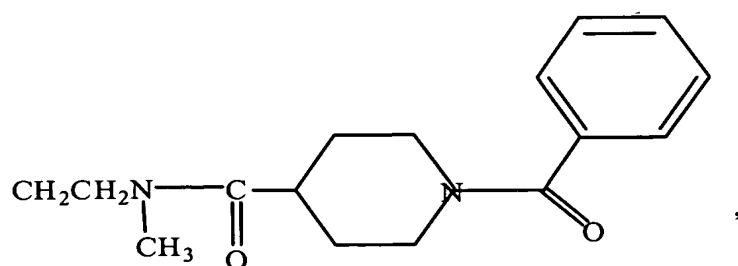
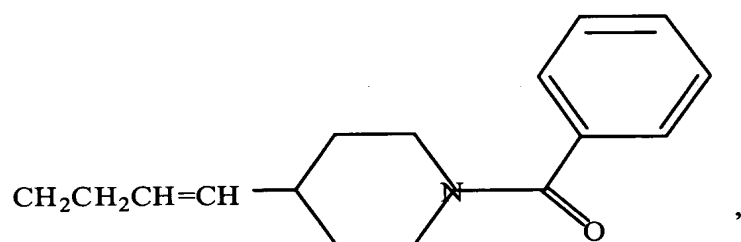
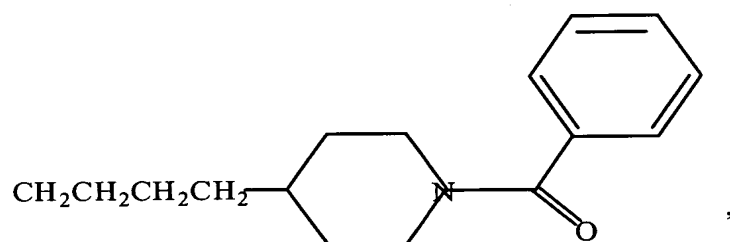
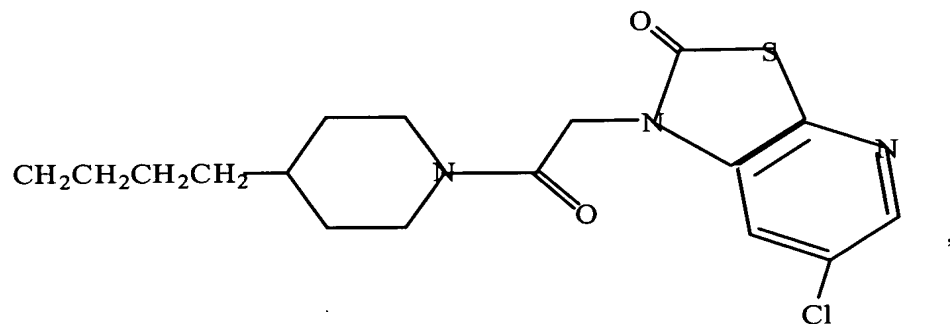
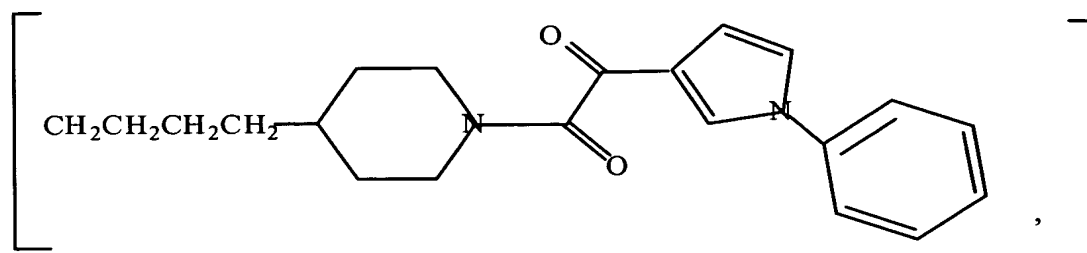


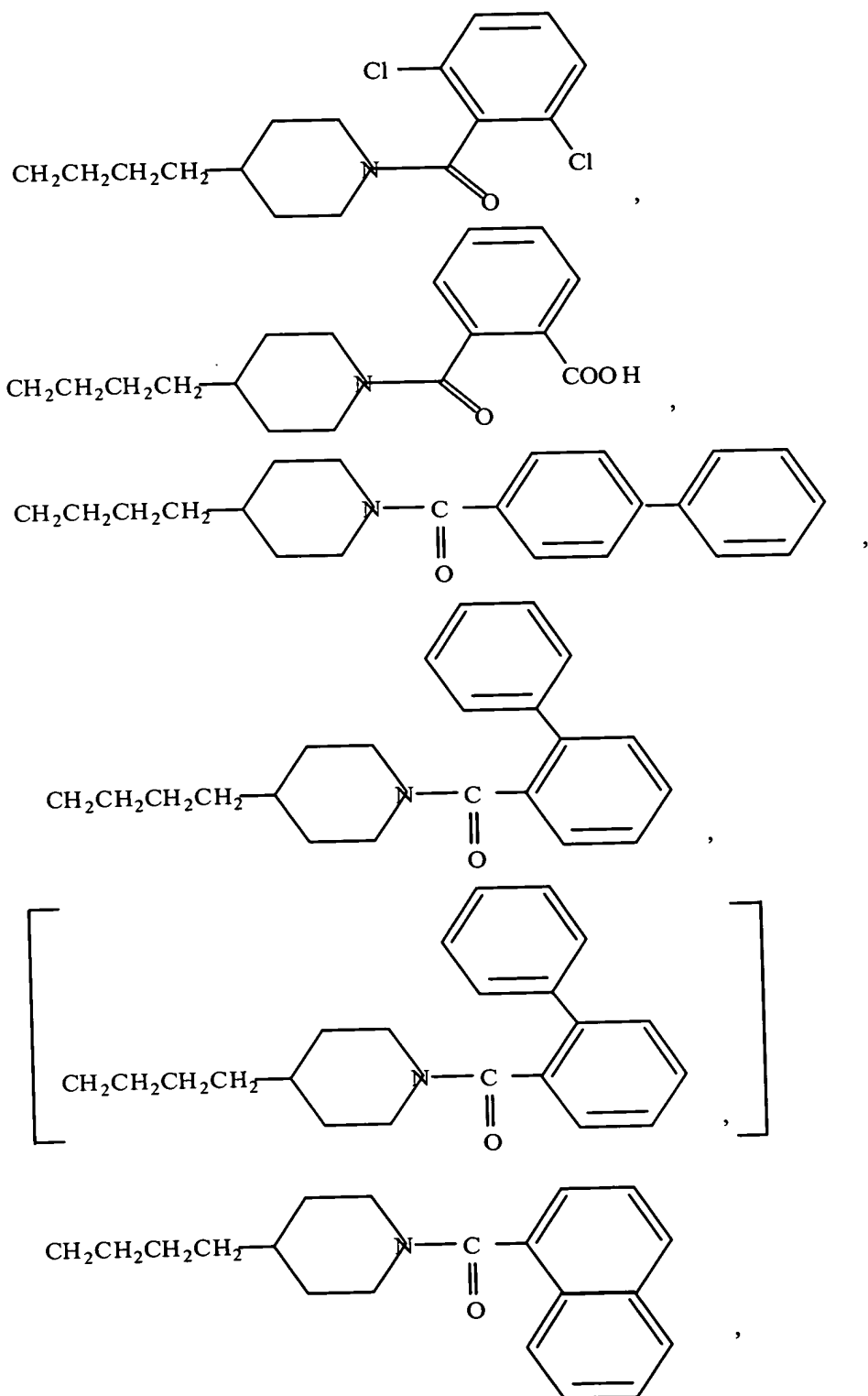


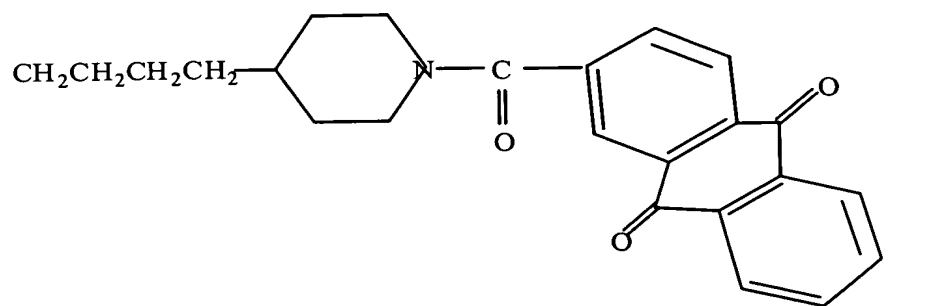
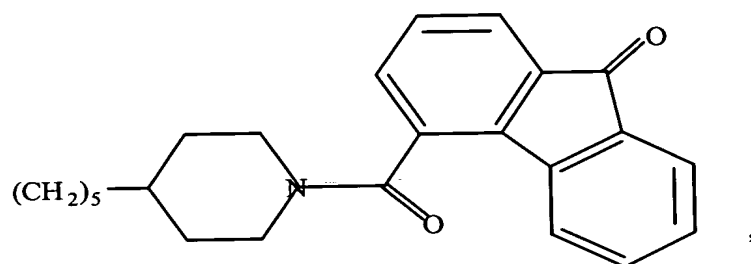
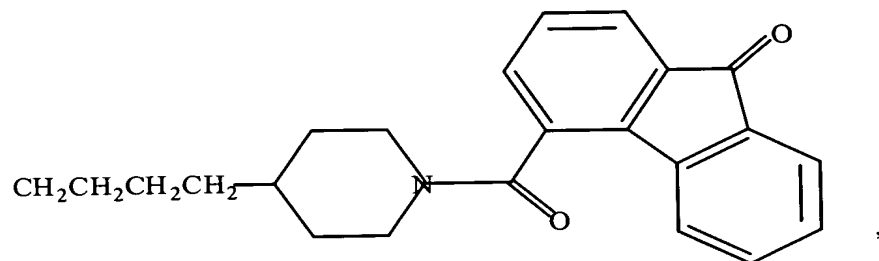
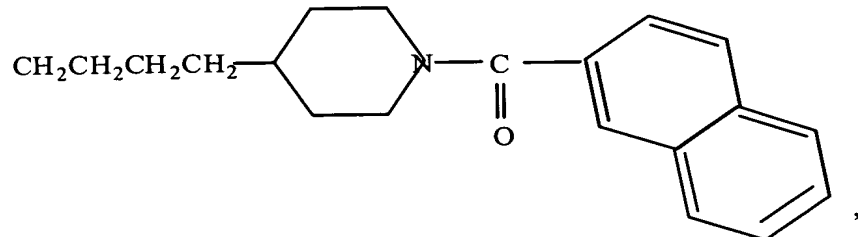
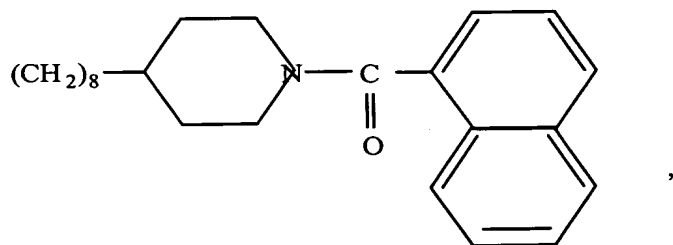


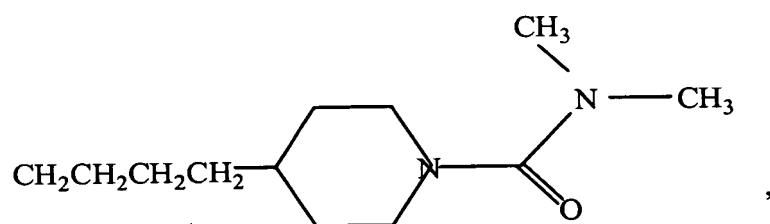
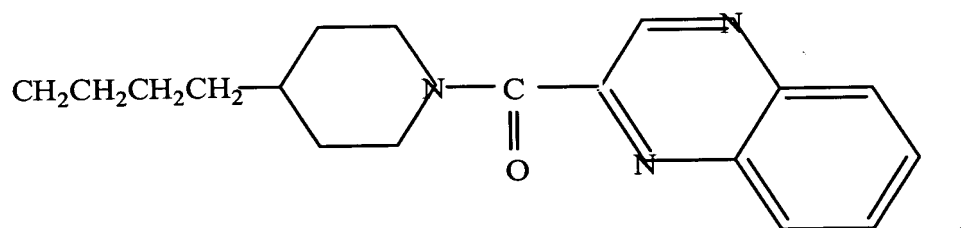
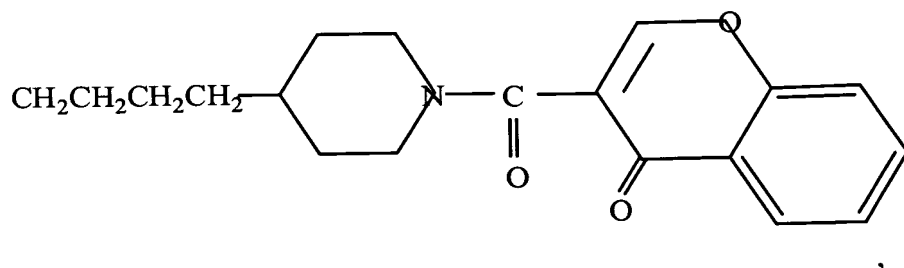
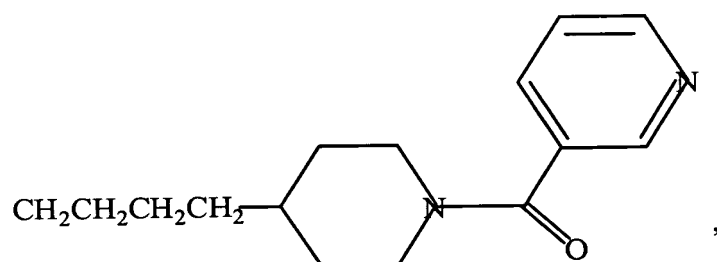
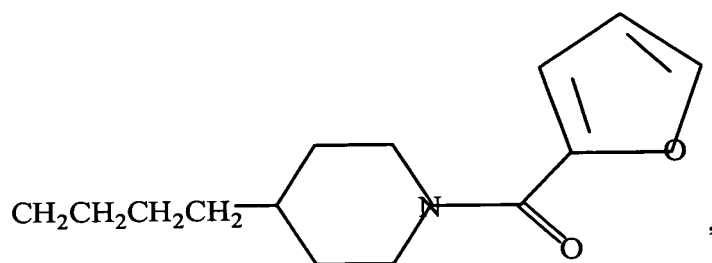


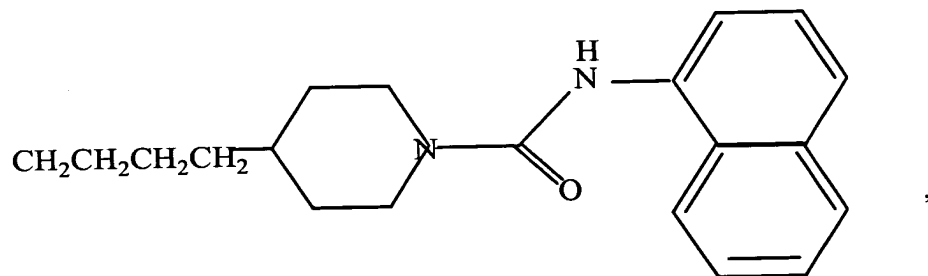
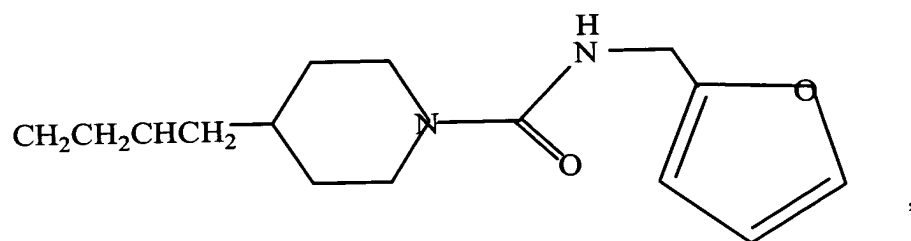
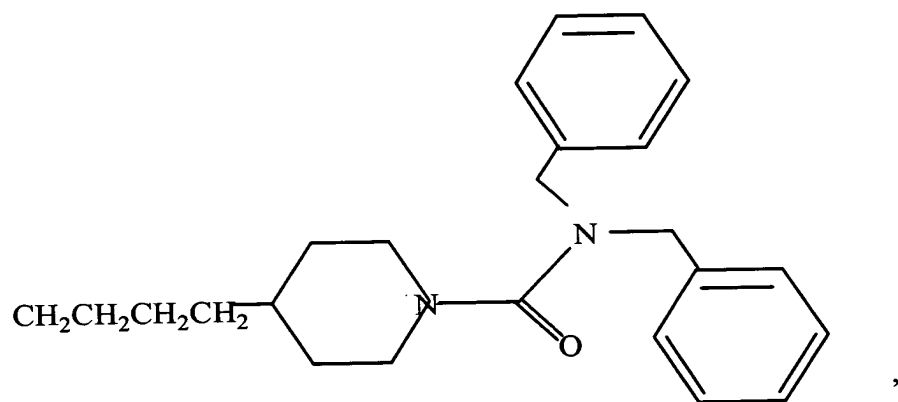
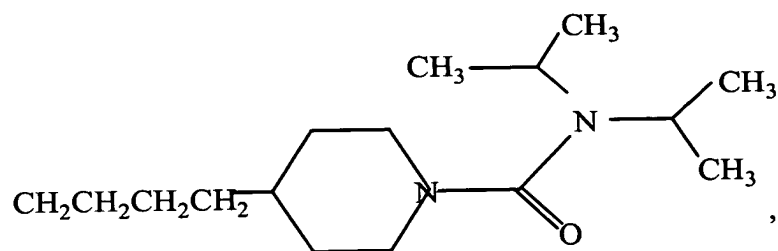


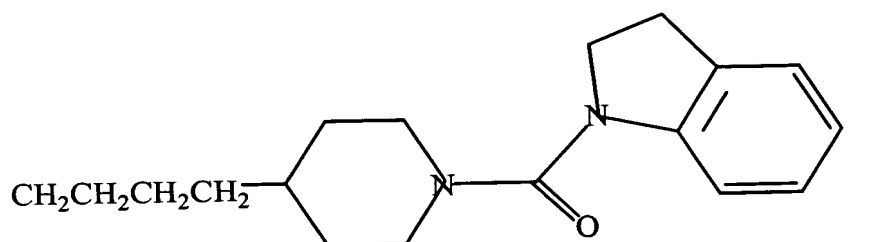
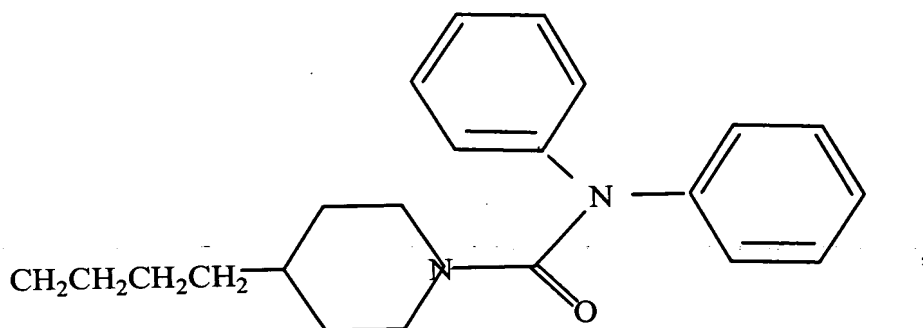
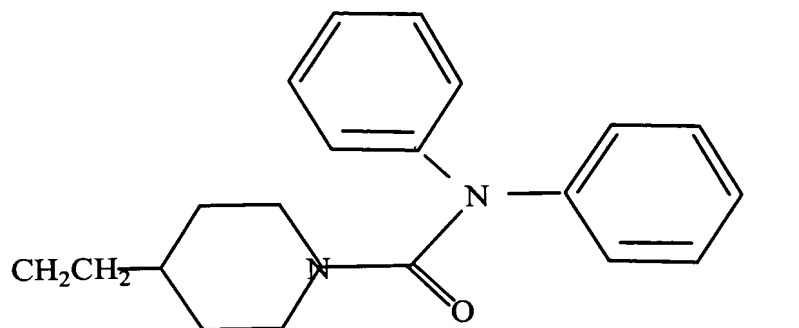
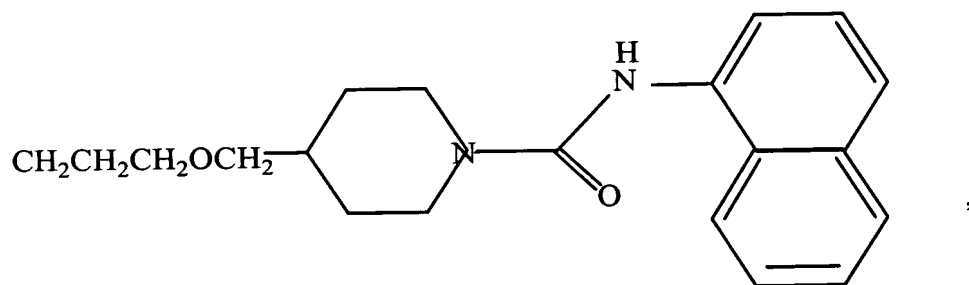


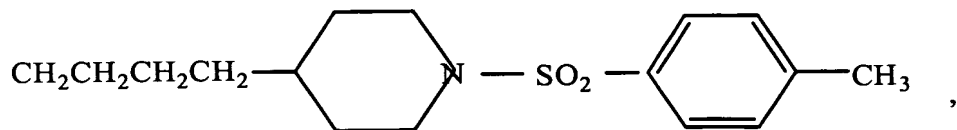
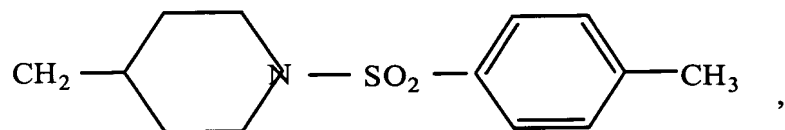
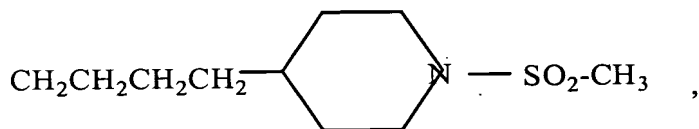
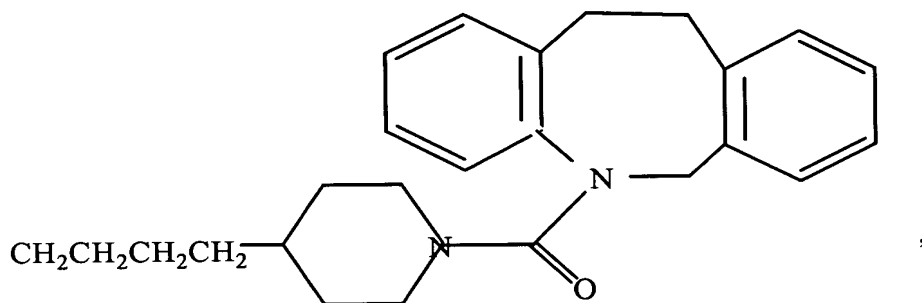
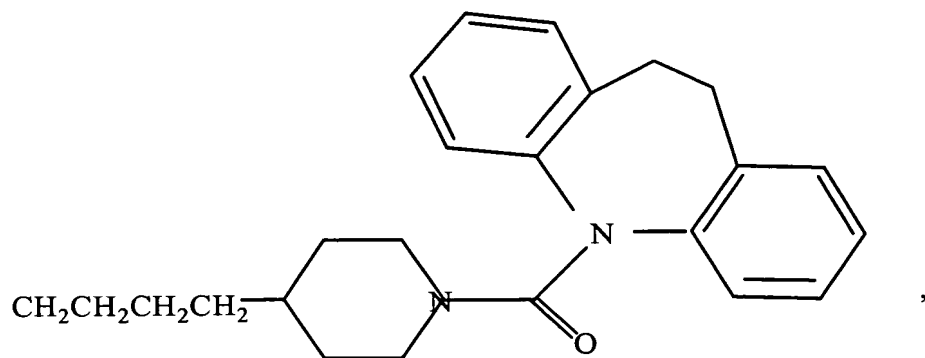


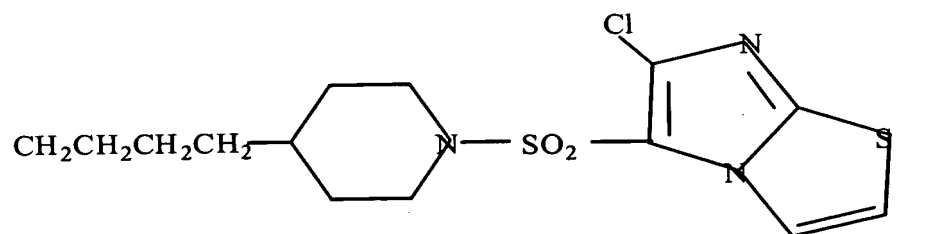
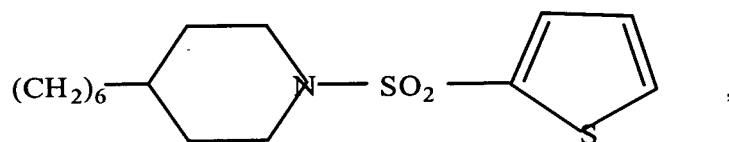
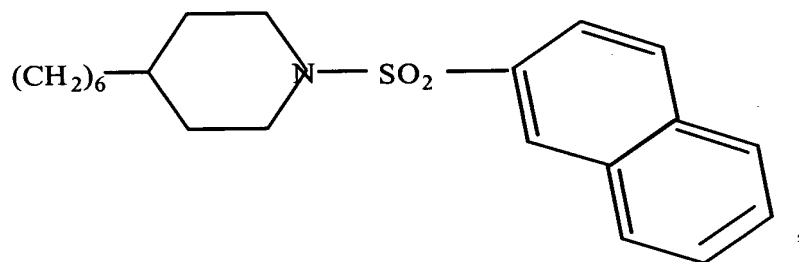
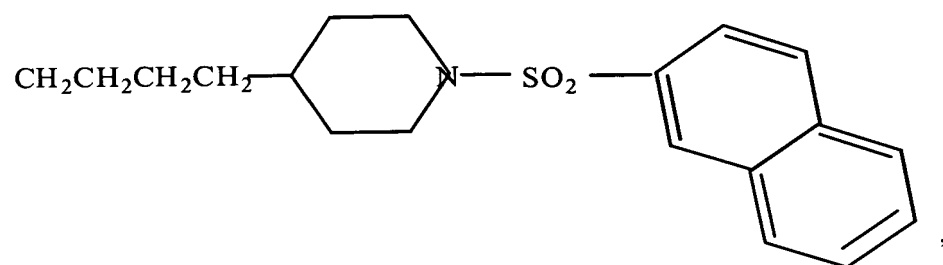
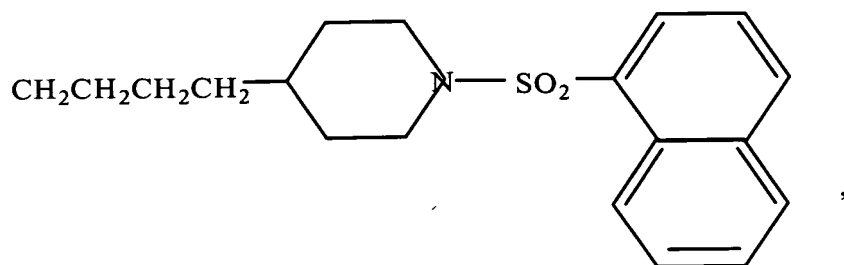


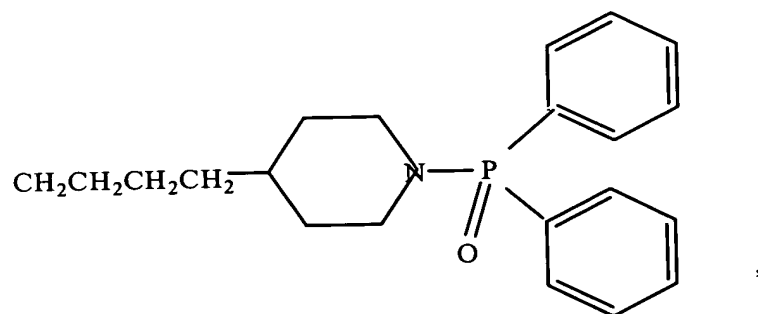
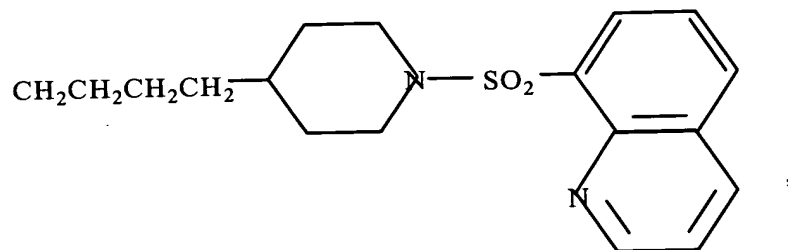
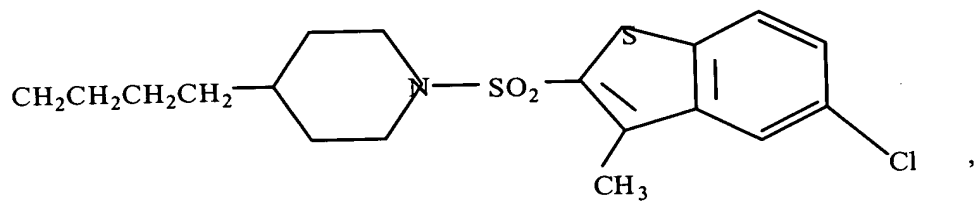
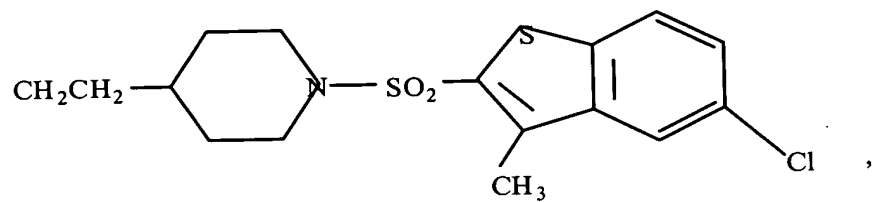


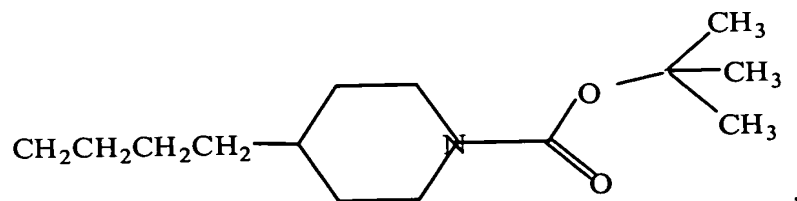
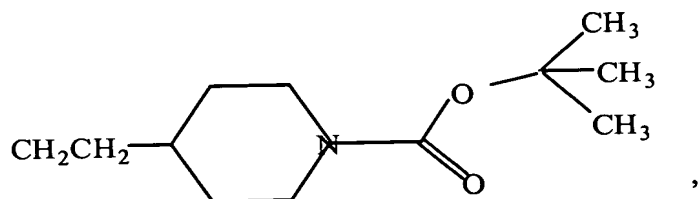
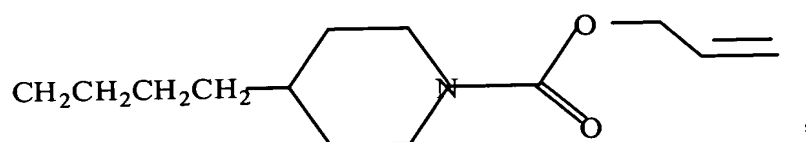
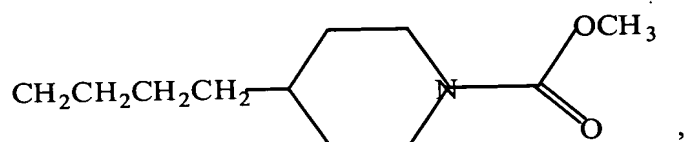
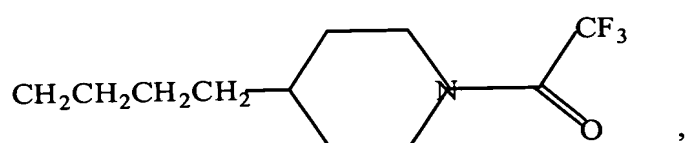
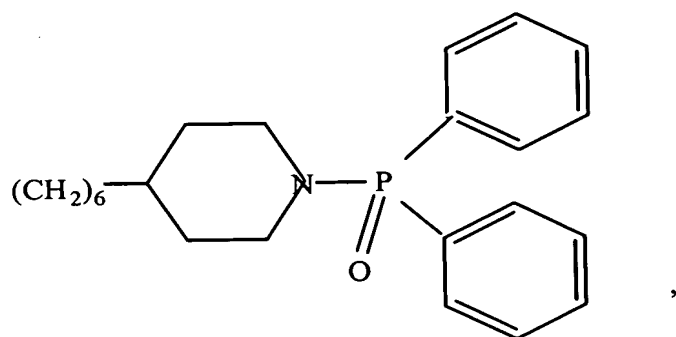


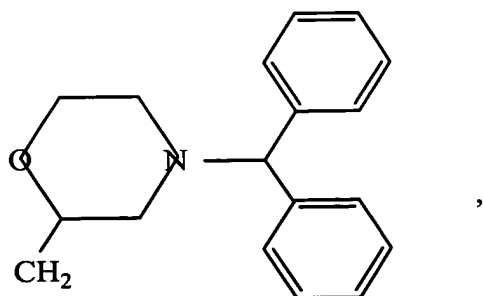
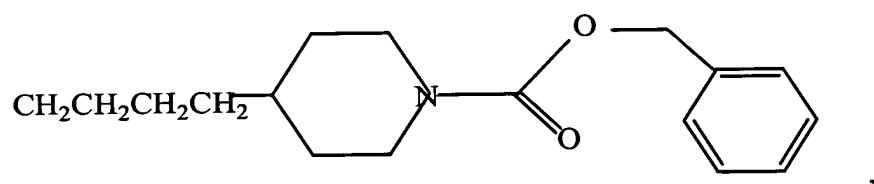
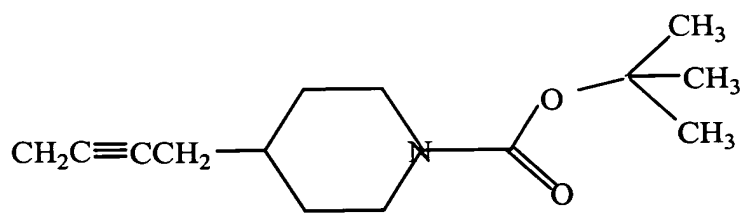
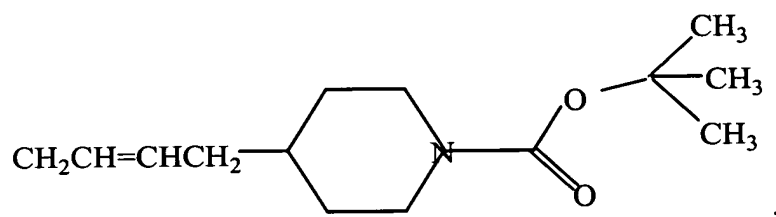
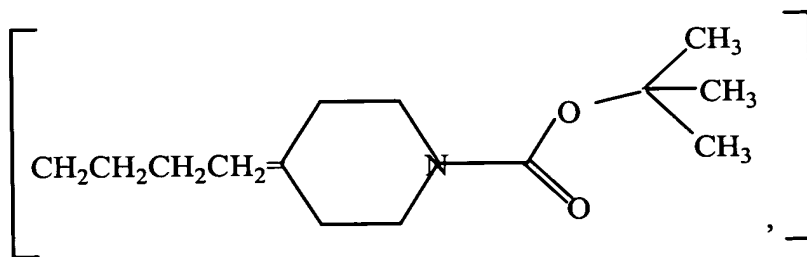


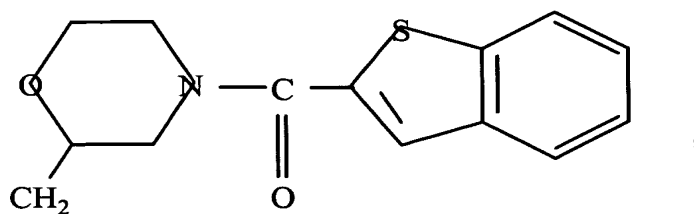
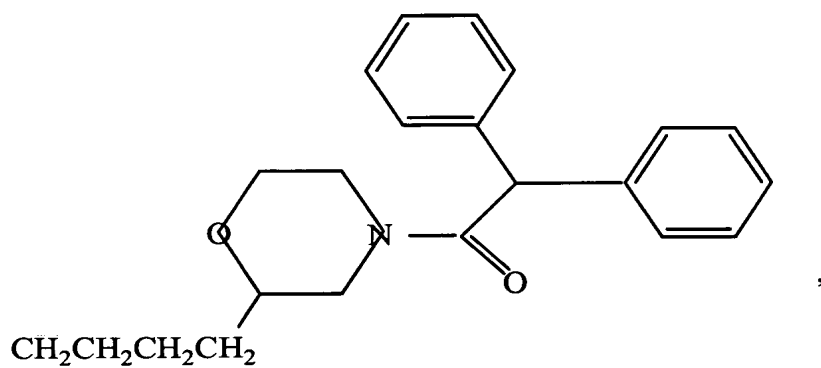
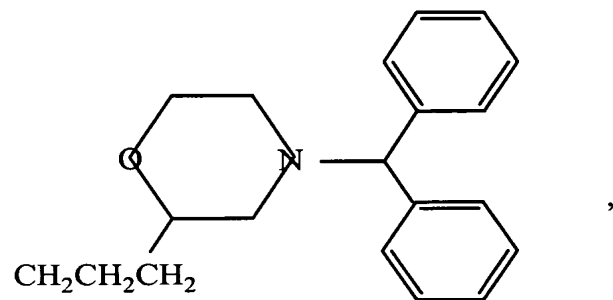
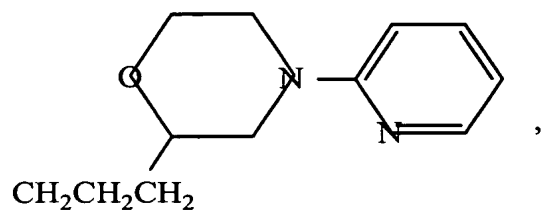


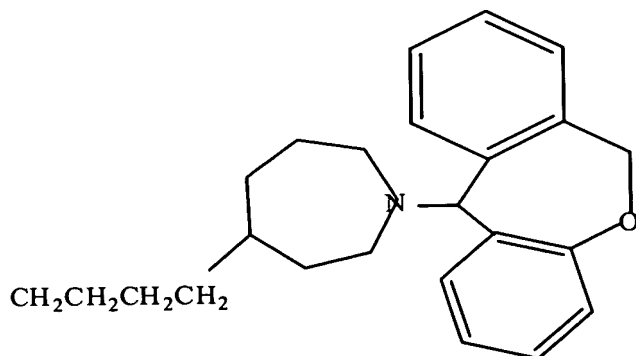
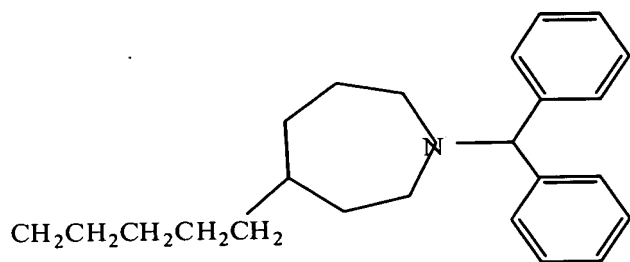
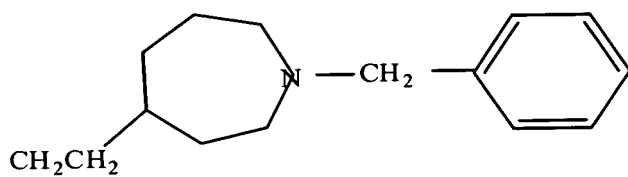
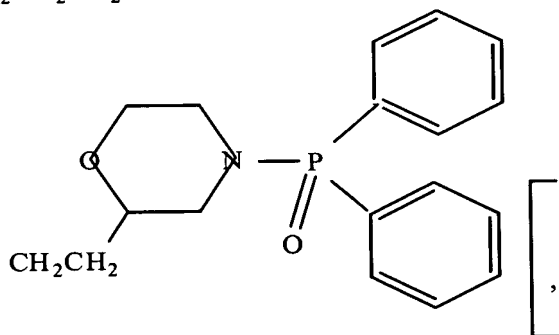


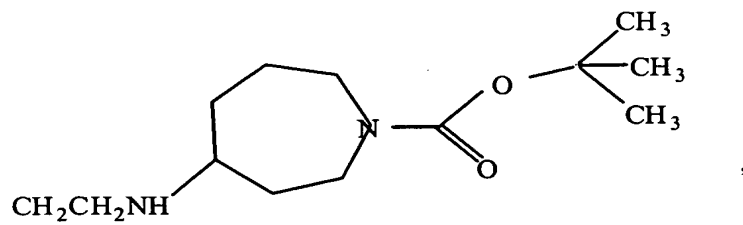
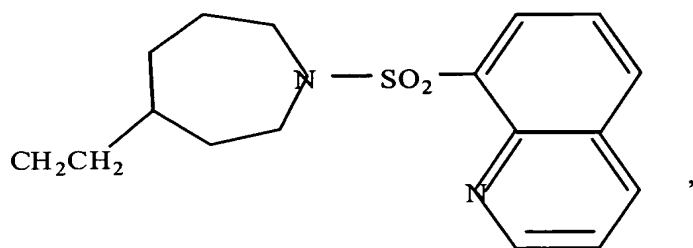
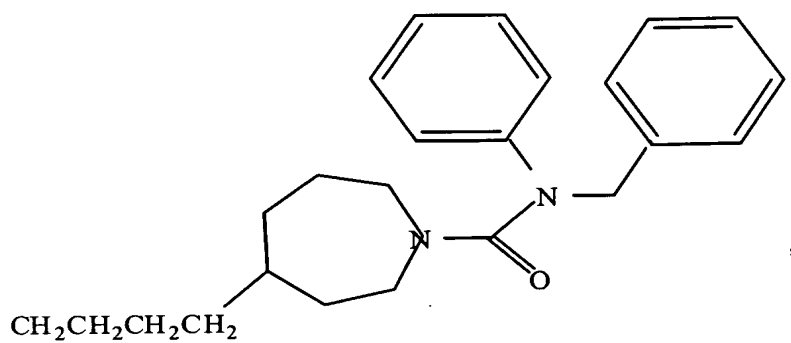
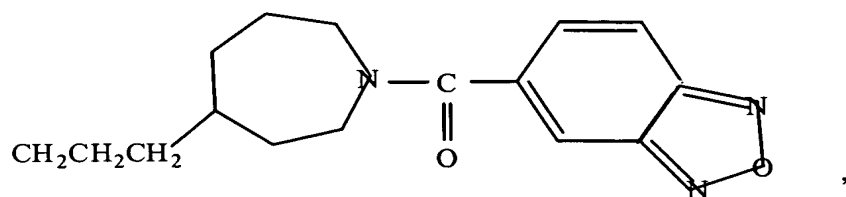
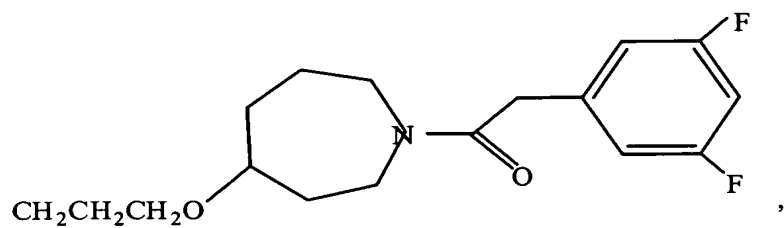


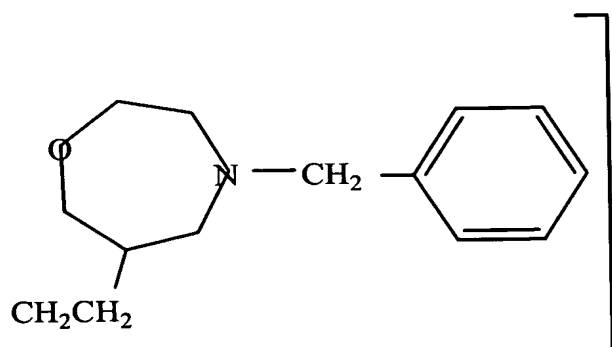
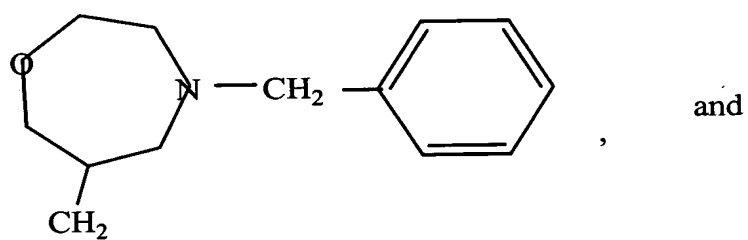
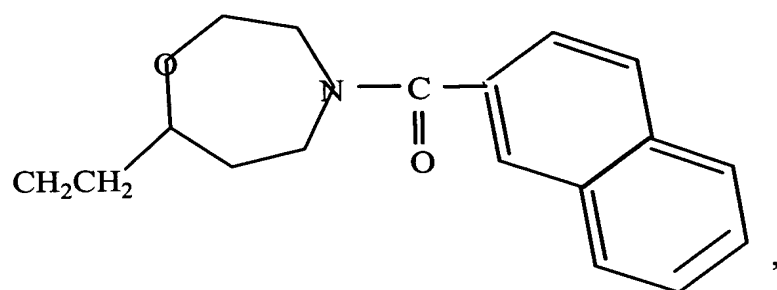
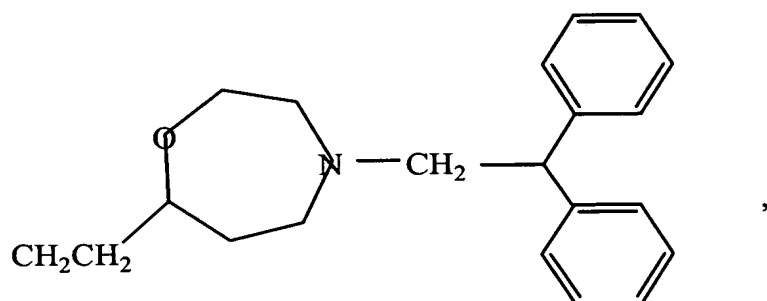






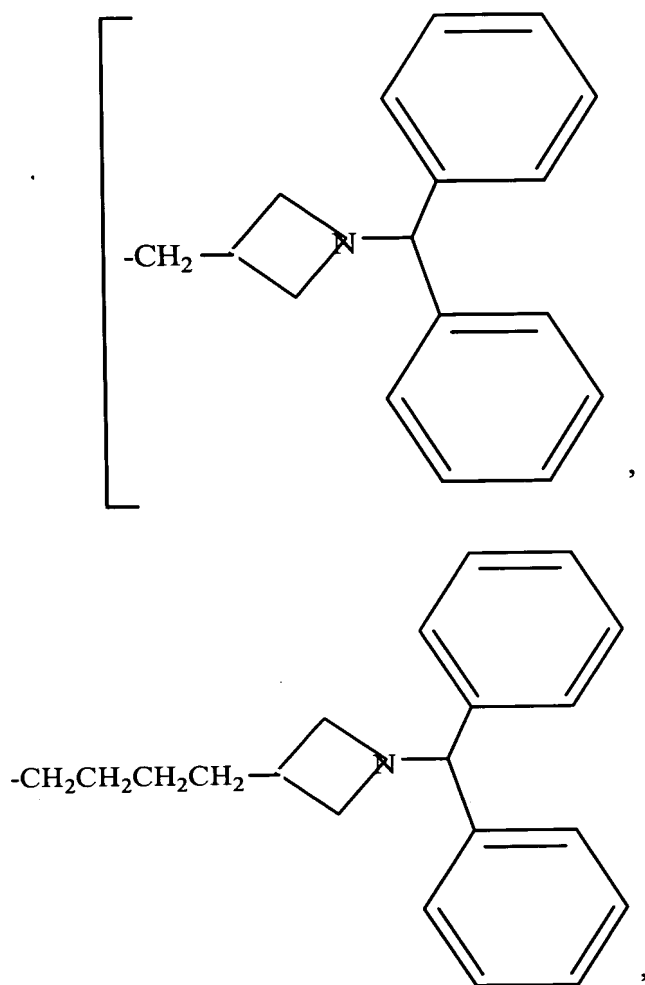


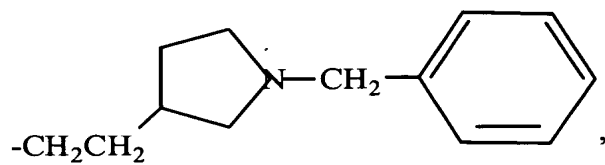
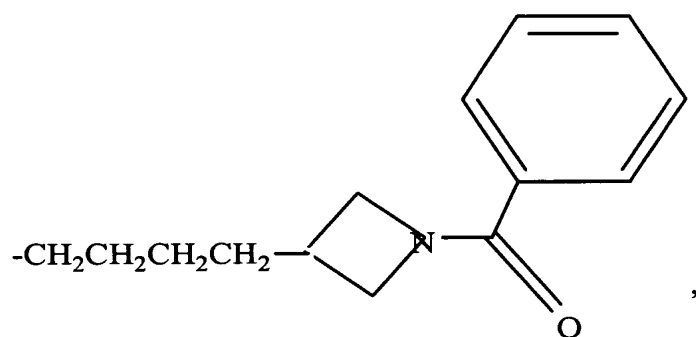
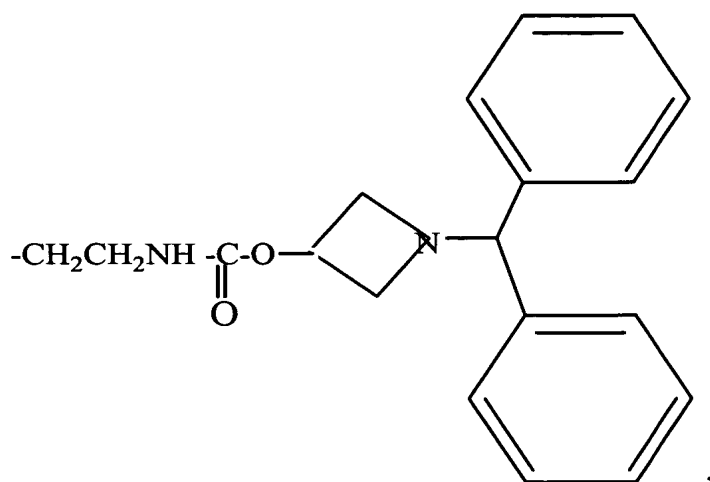


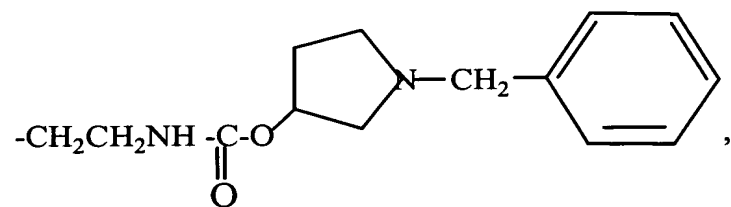
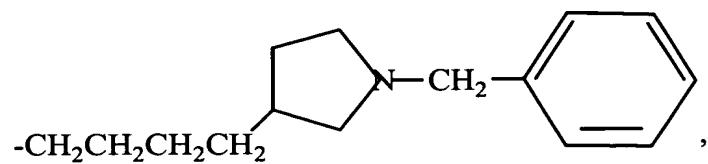
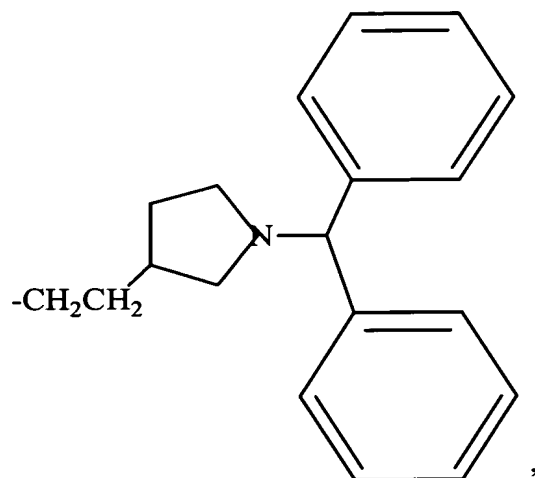


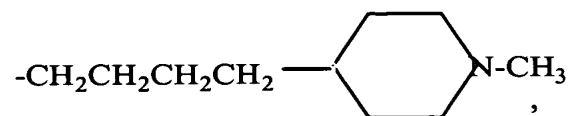
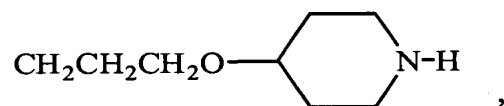
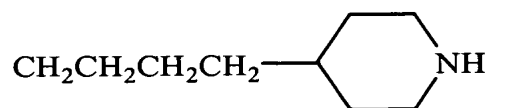
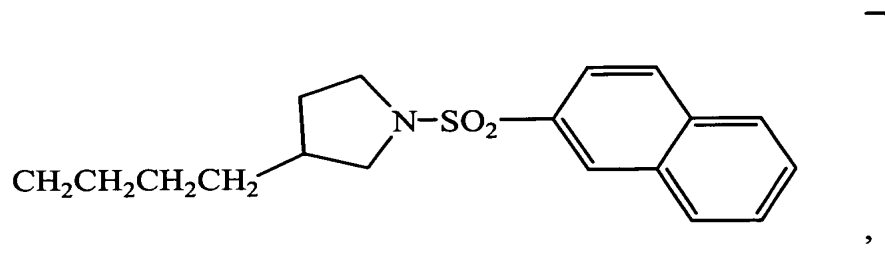
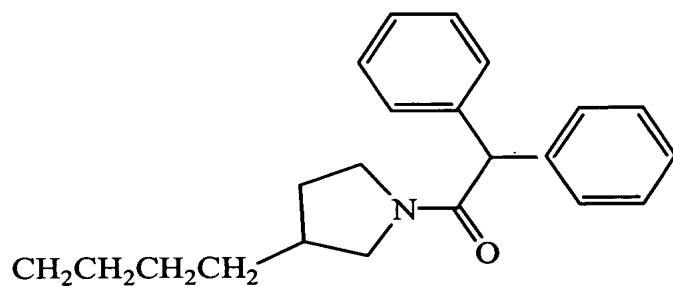
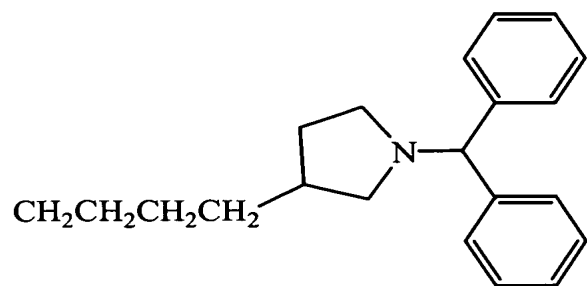
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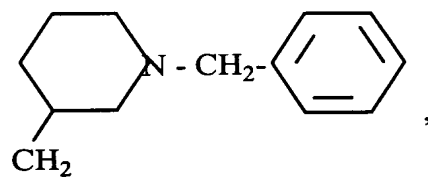
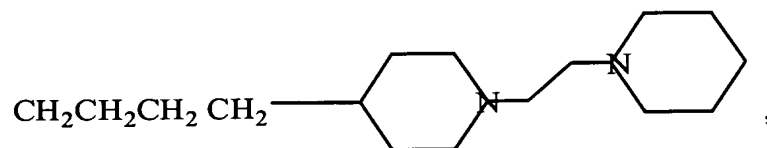
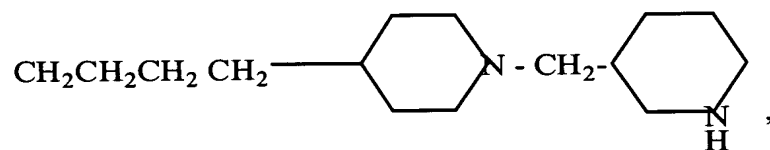
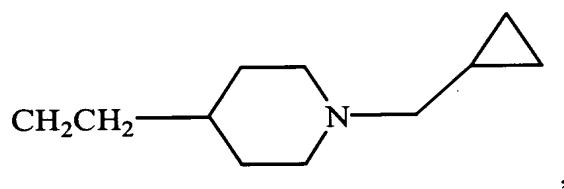
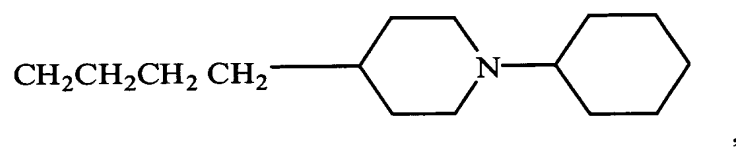
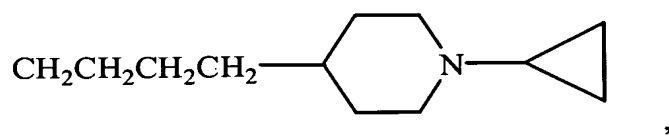
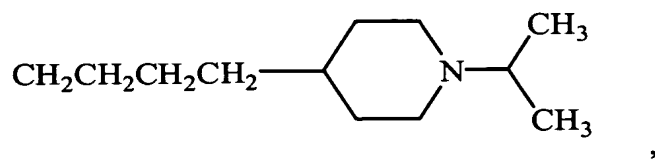
82. A method of suppressing autoimmune disease according to claim 65, wherein DEG is selected from the group consisting of

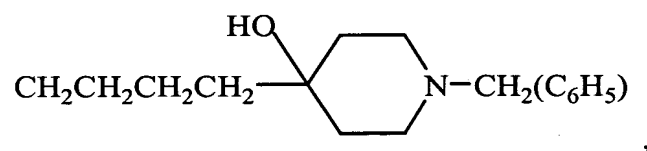
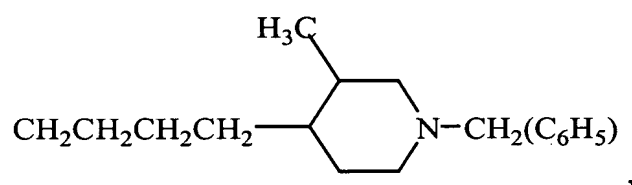
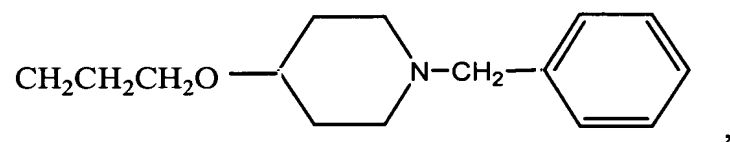
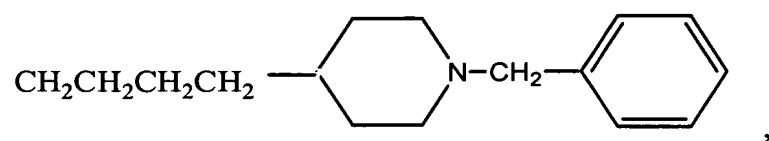
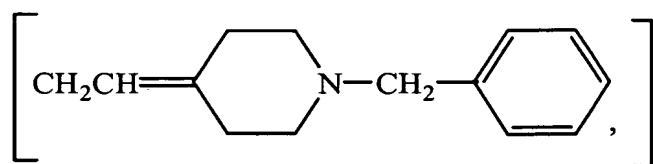


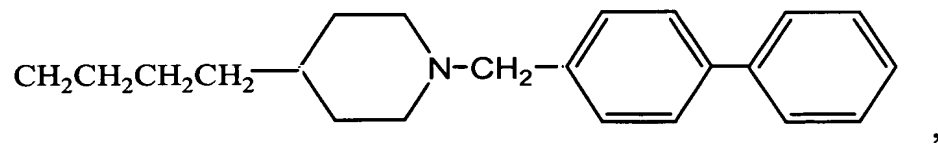
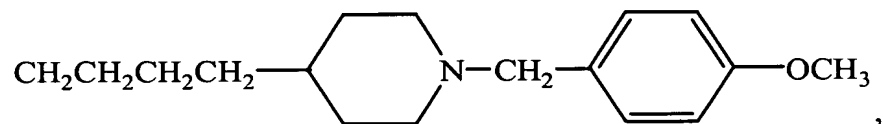
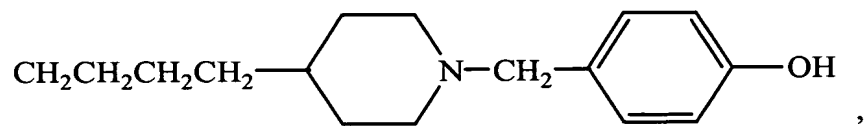
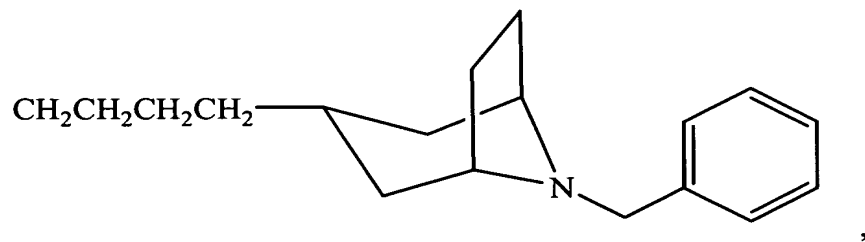
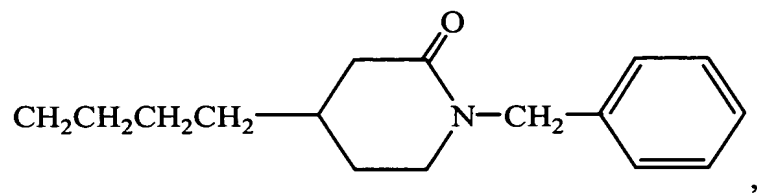


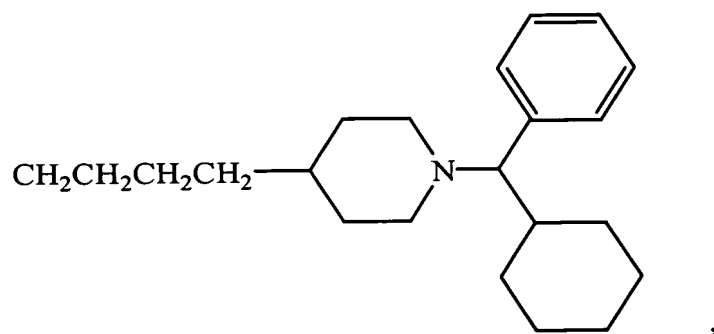
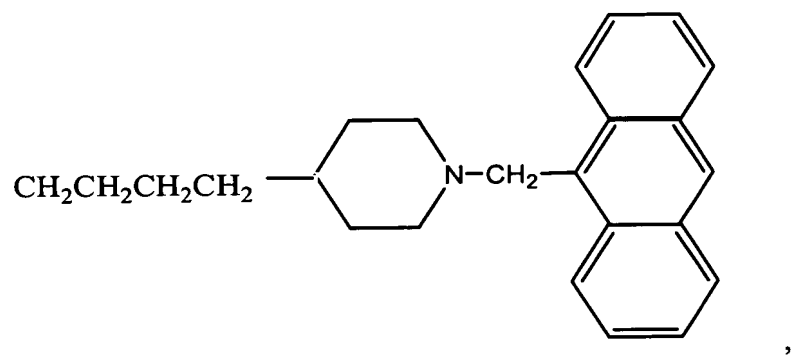


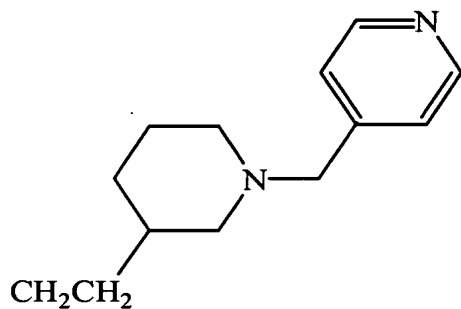




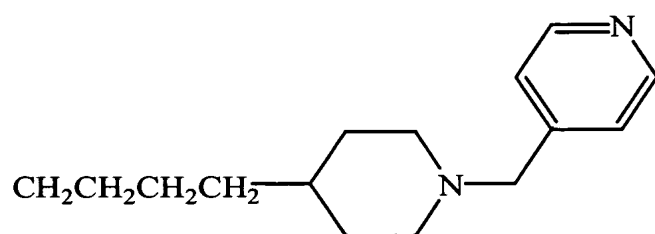




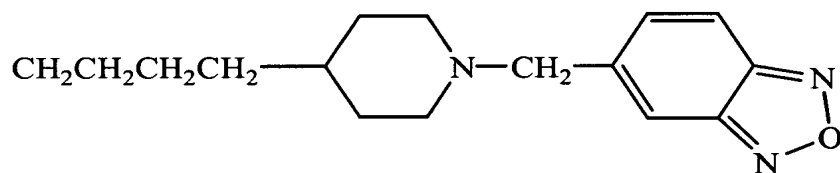




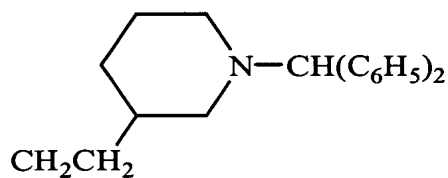
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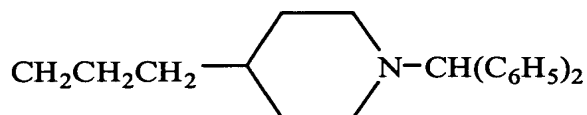
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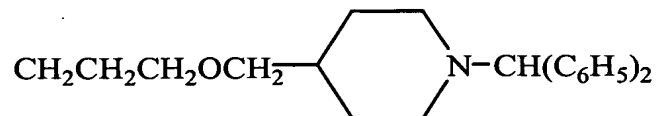
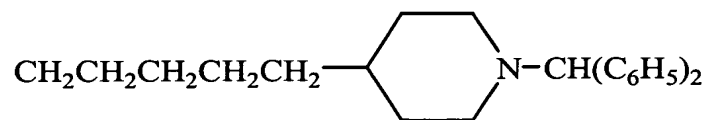
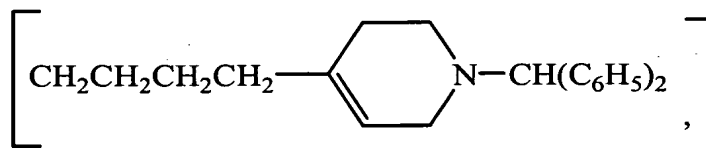
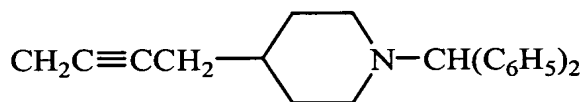
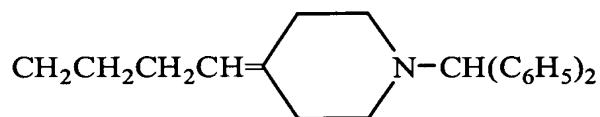
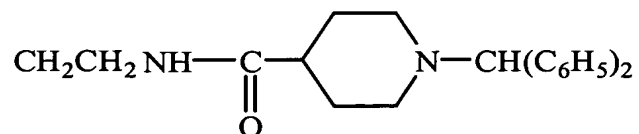
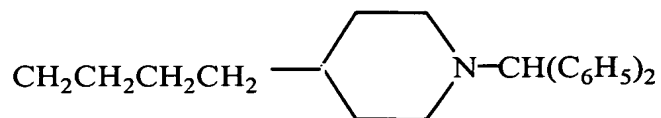
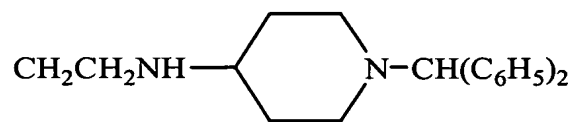
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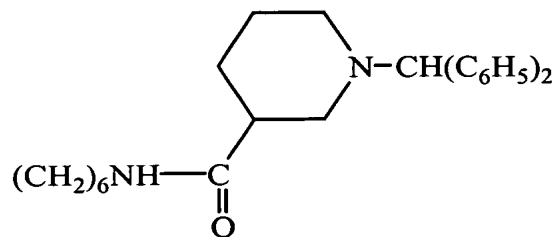
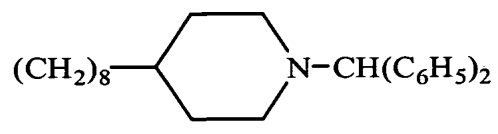
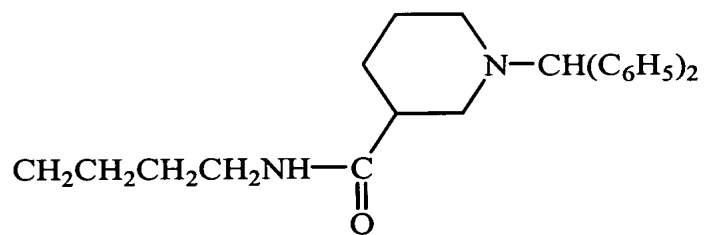
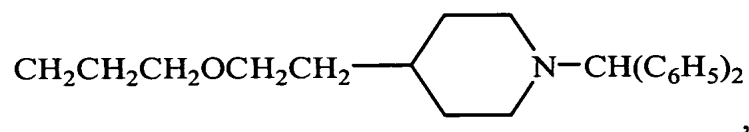
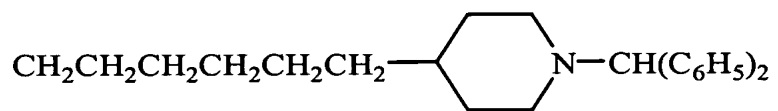
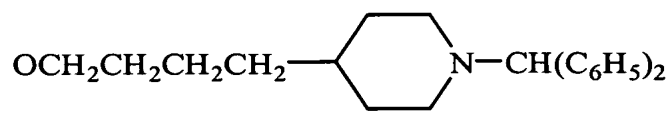


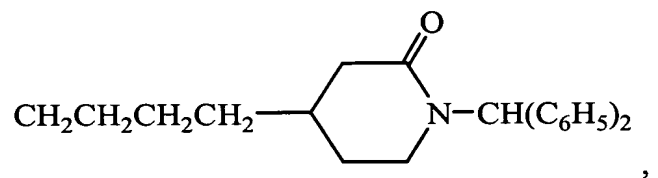
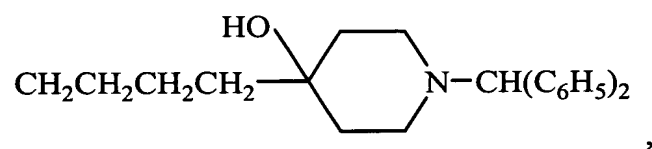
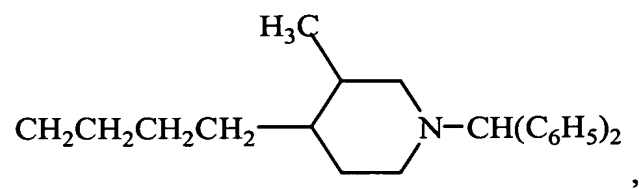
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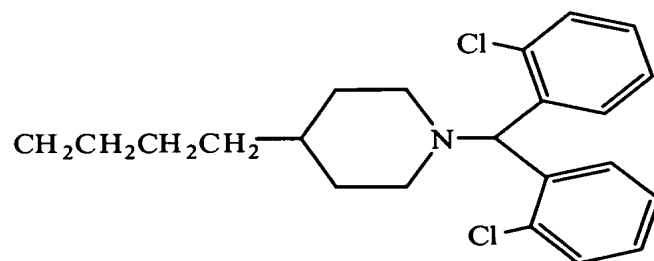
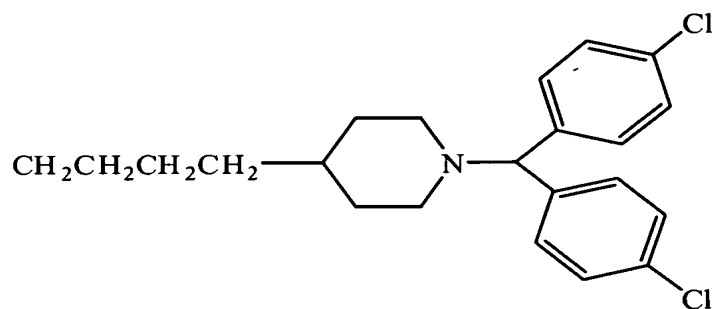
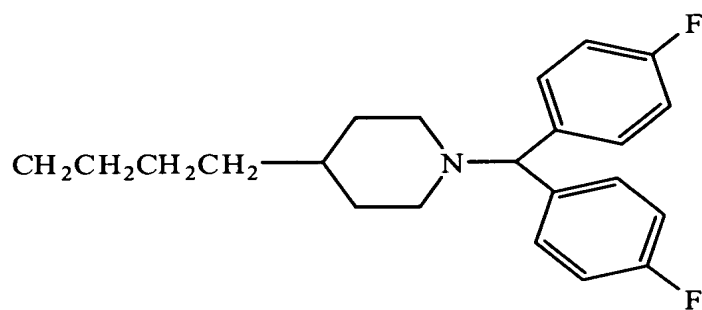
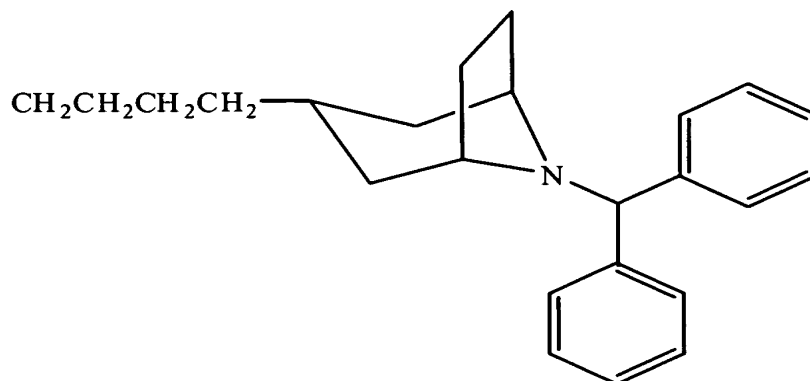


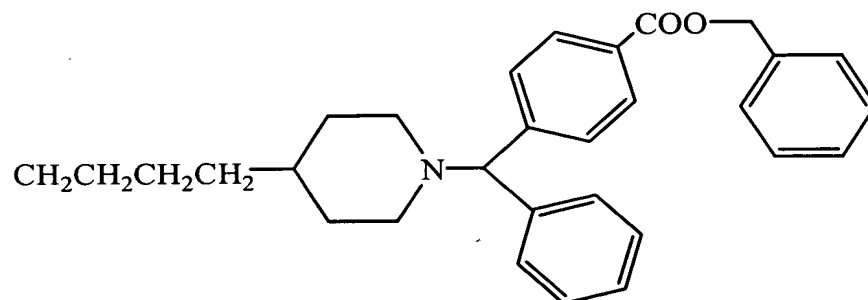
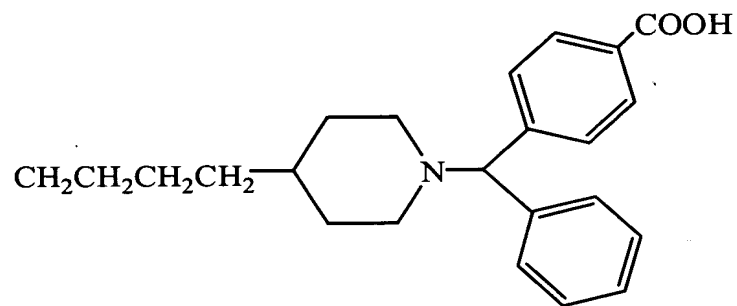
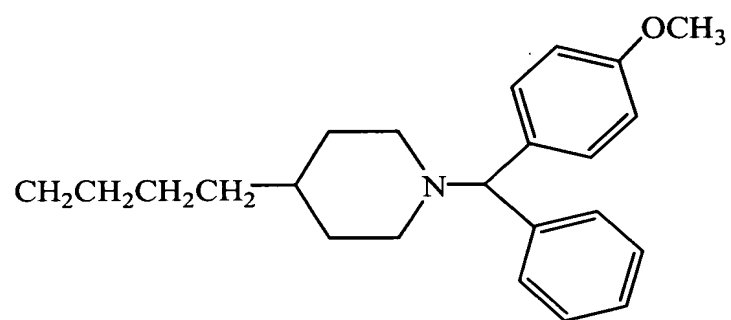
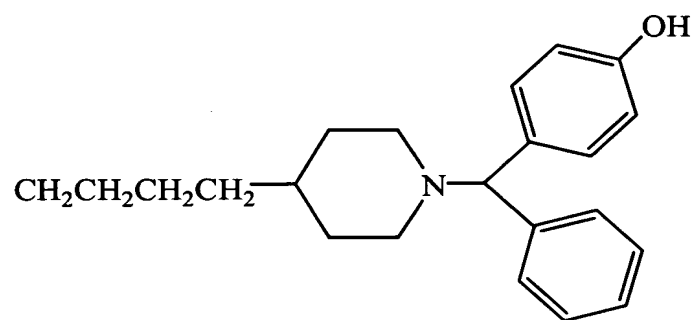
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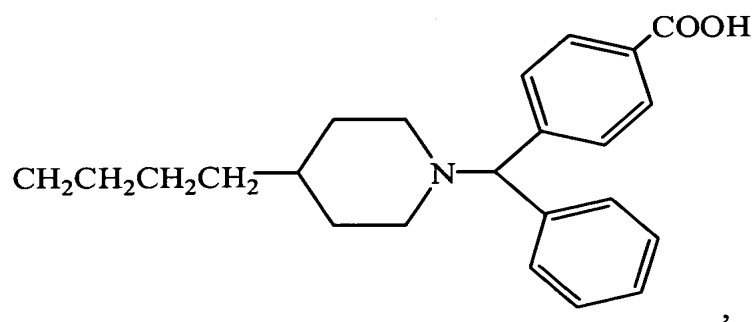
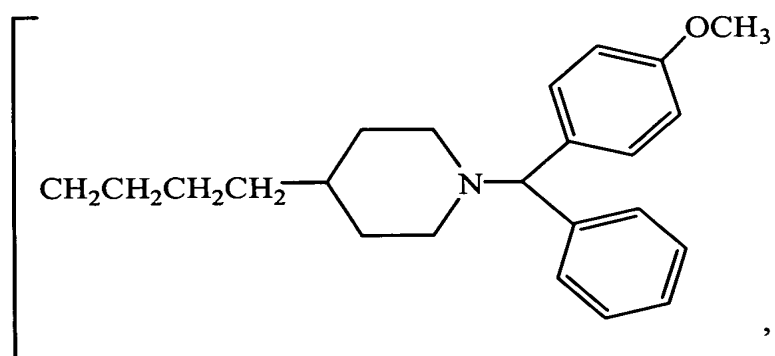
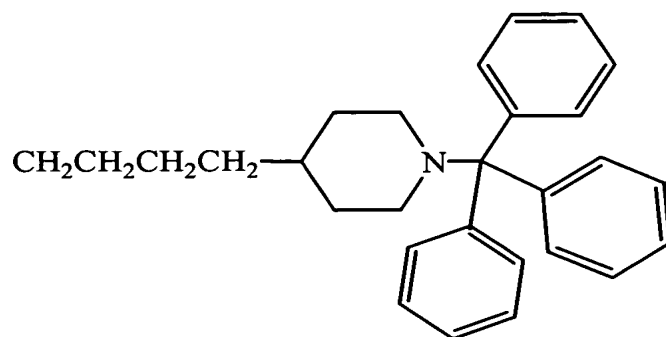


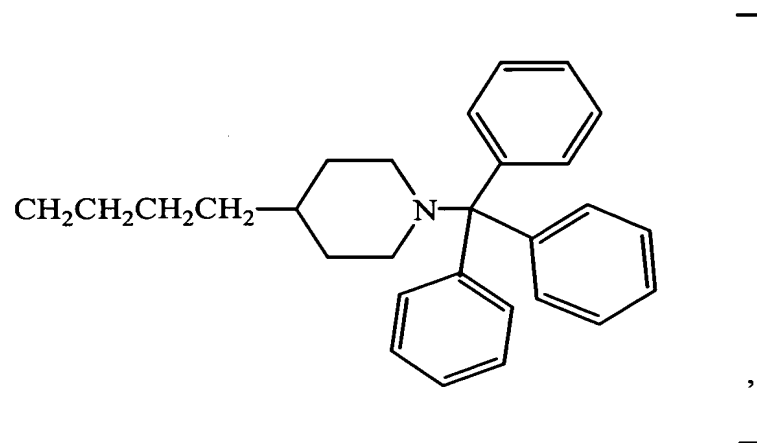
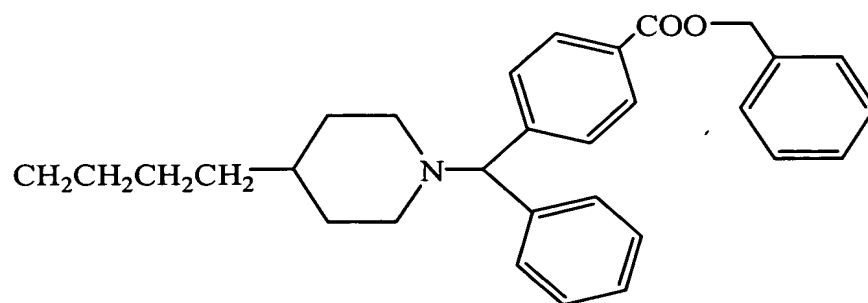


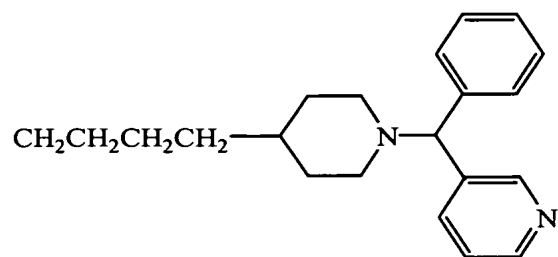




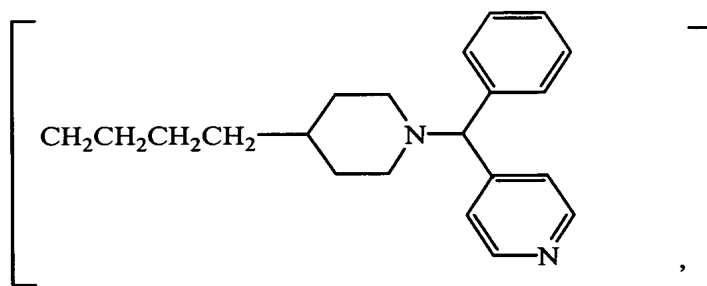




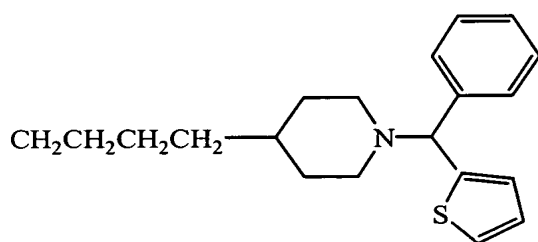




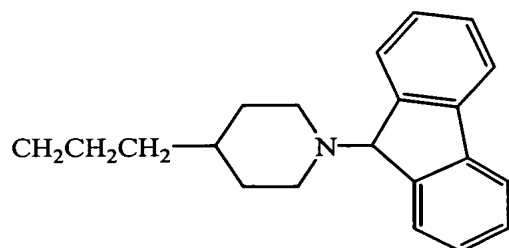
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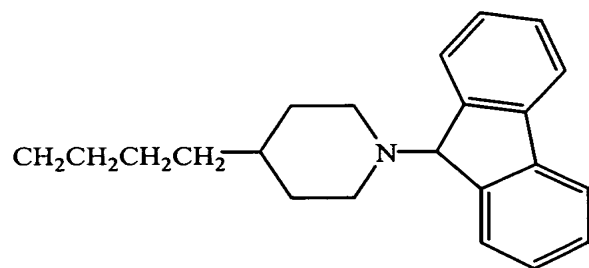
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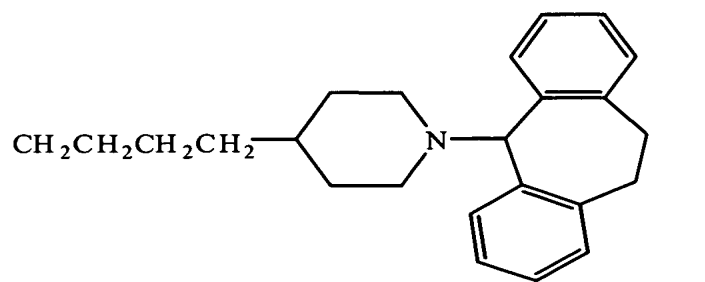
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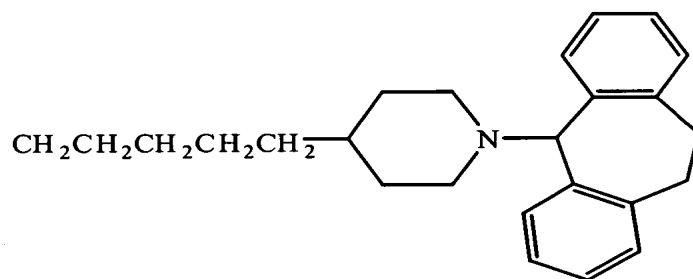
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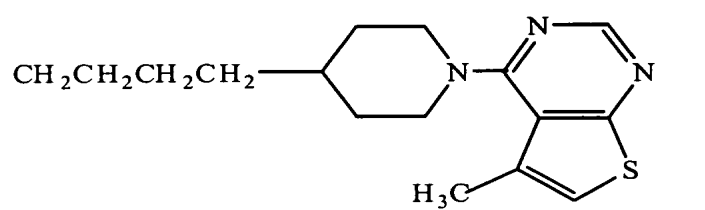
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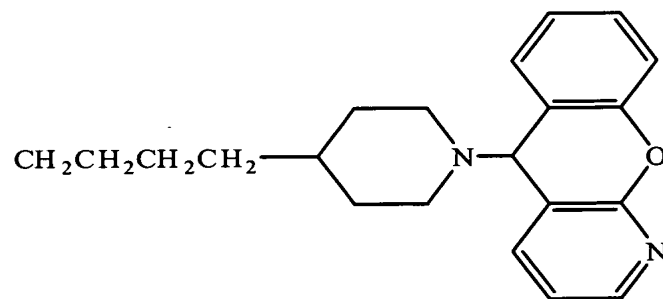
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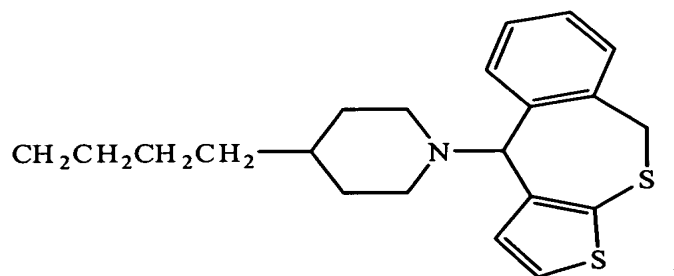
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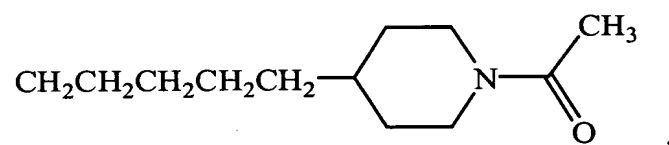
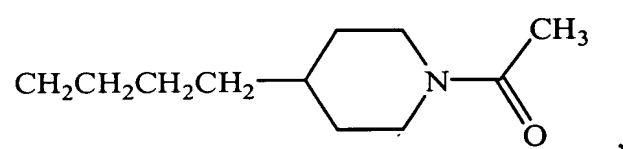
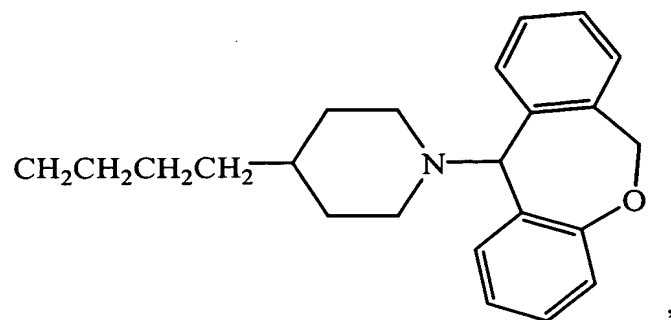
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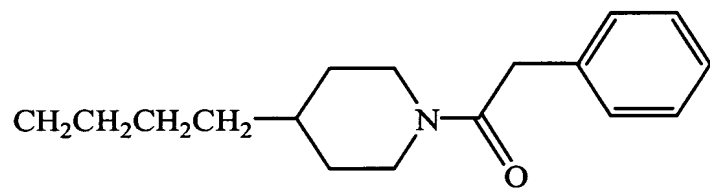
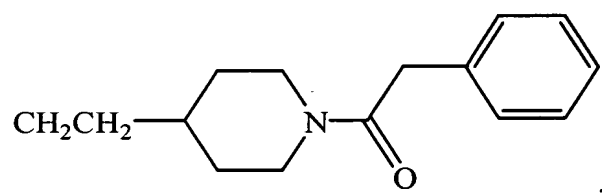
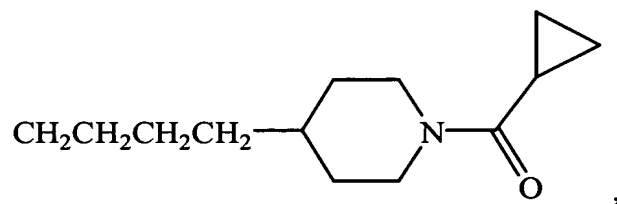
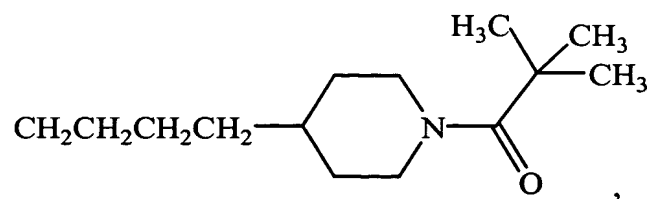


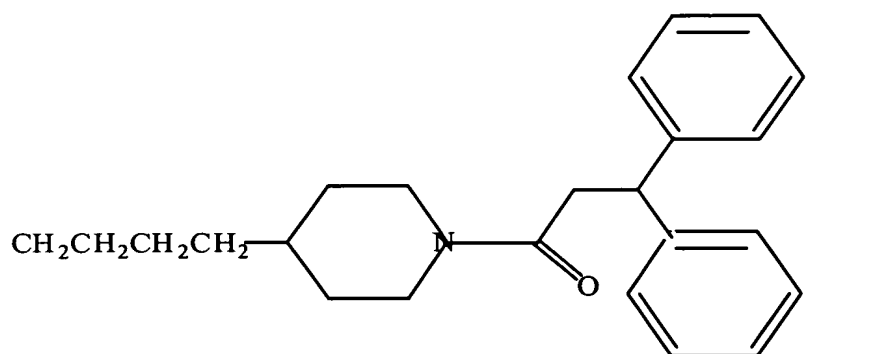
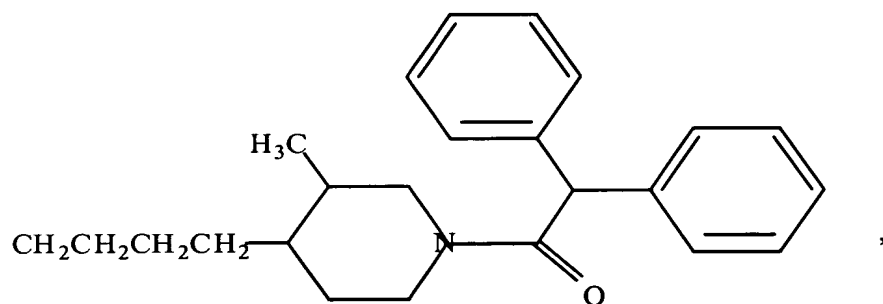
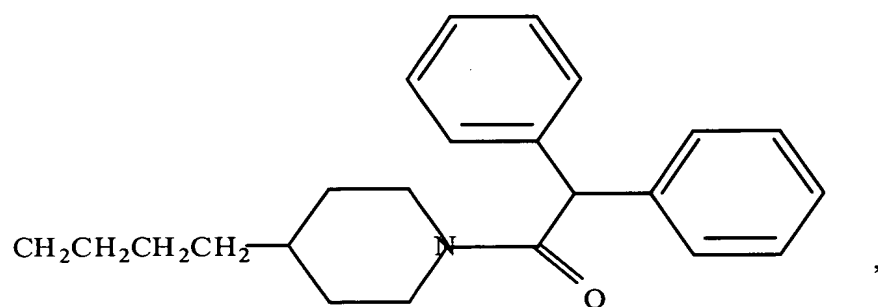
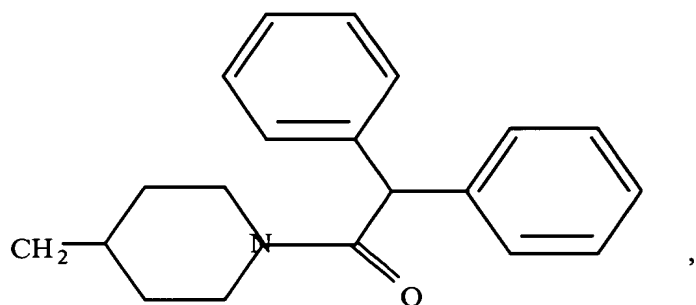
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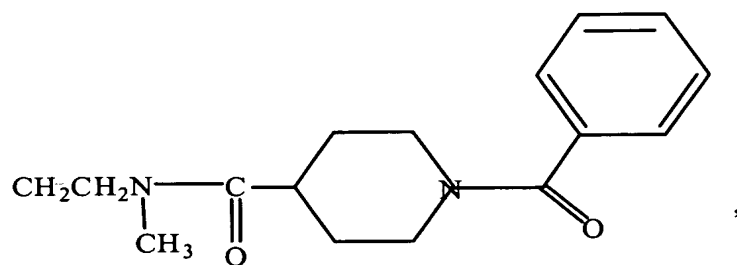
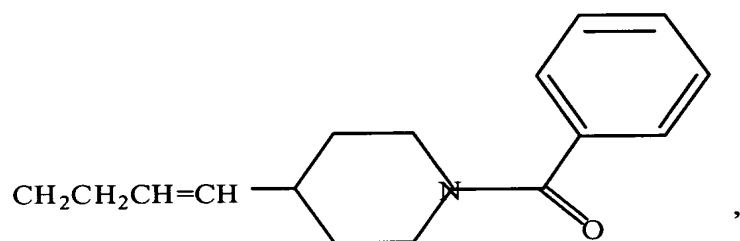
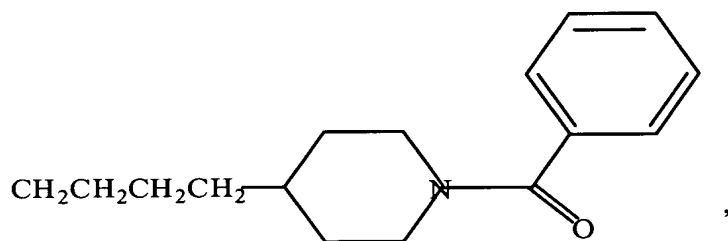
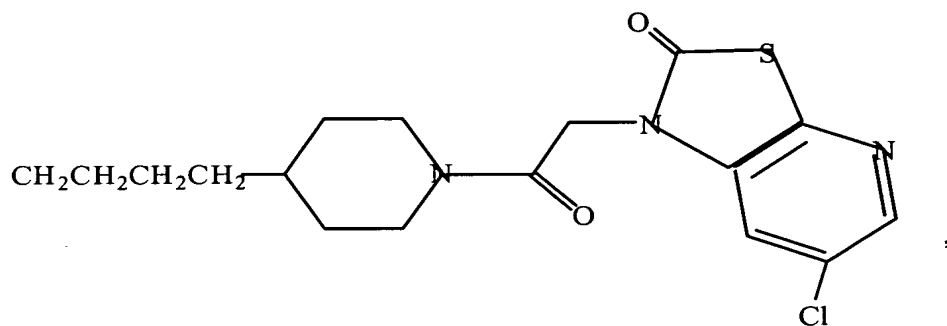
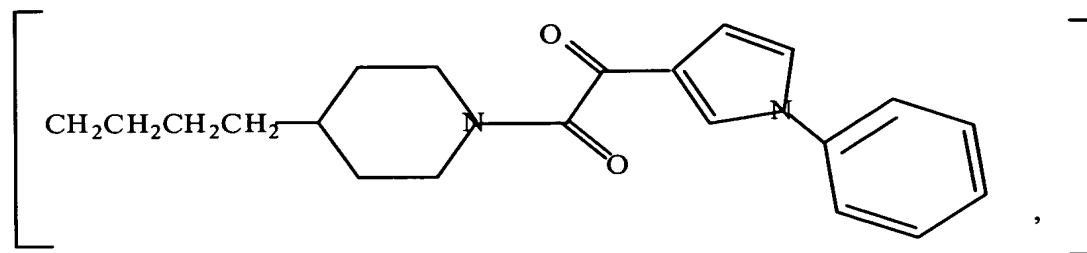


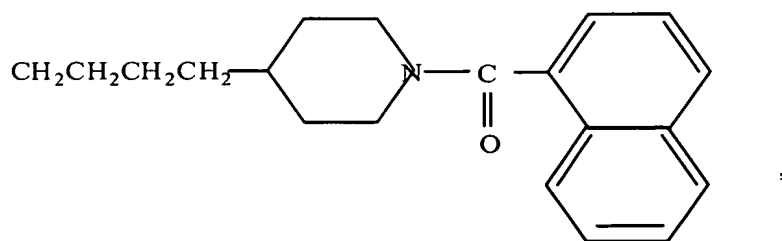
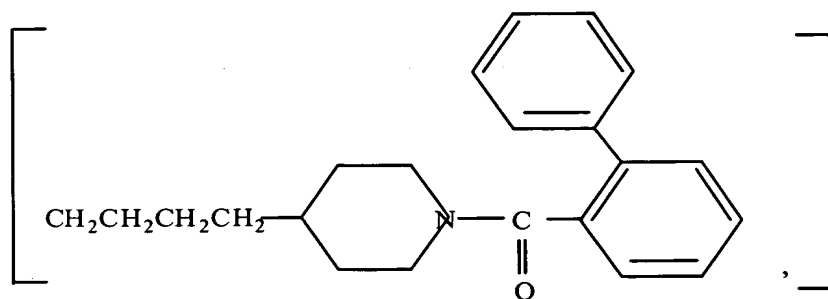
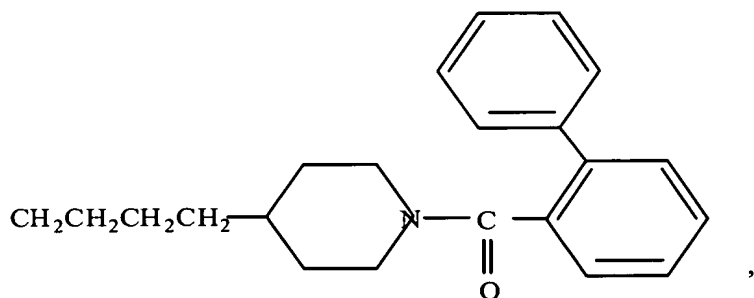
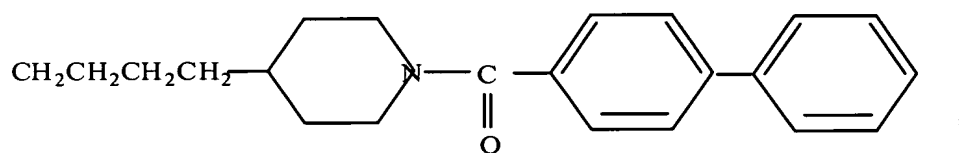
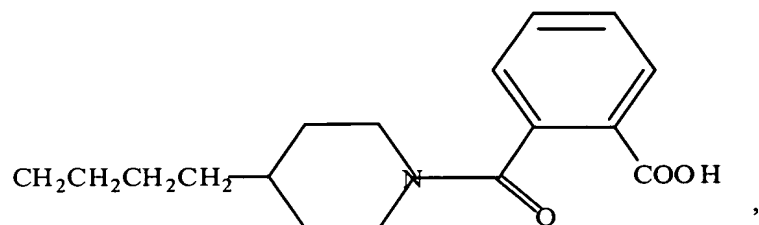
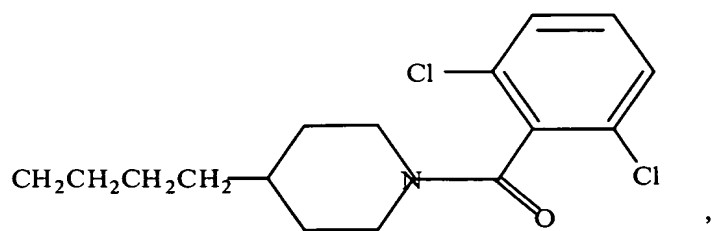
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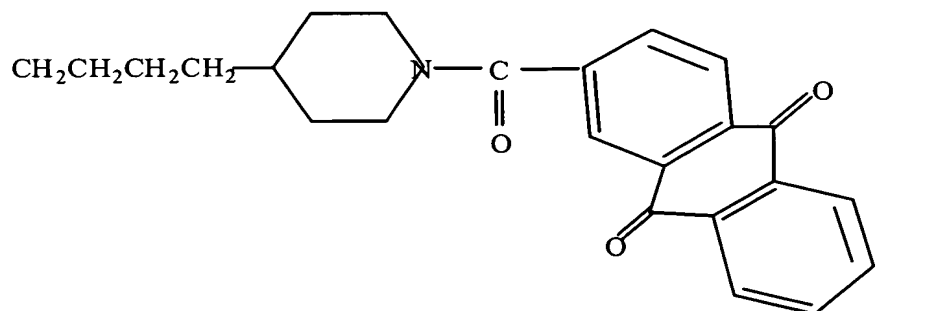
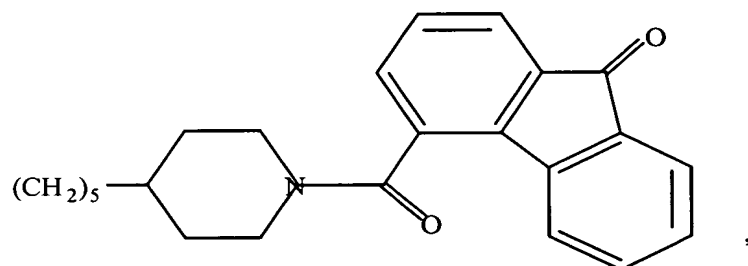
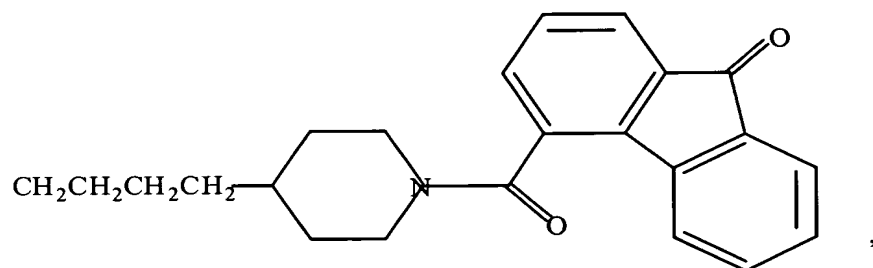
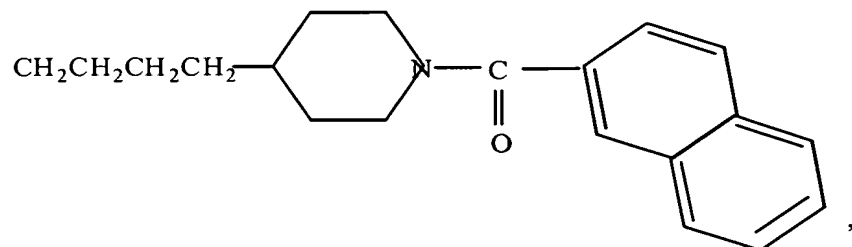
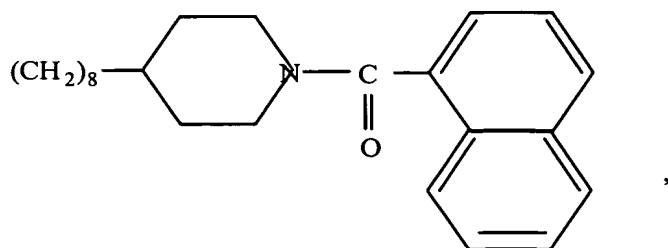


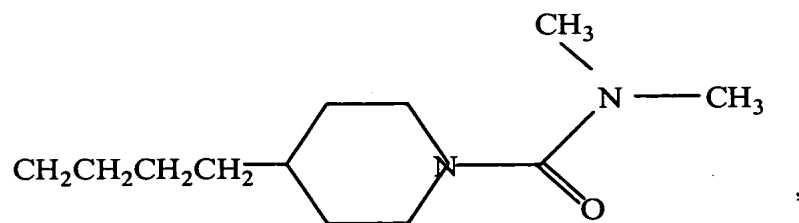
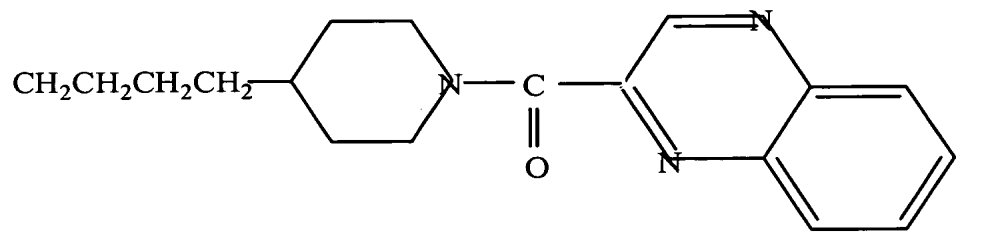
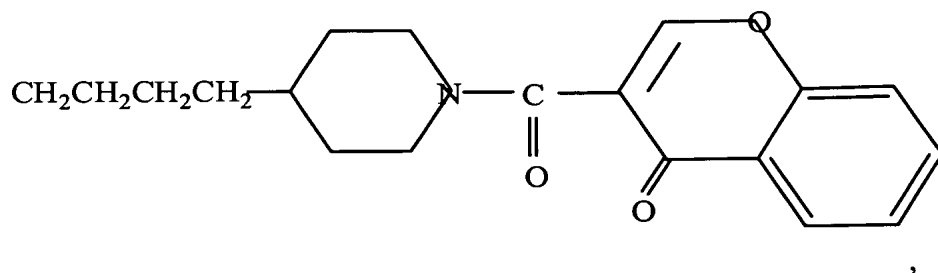
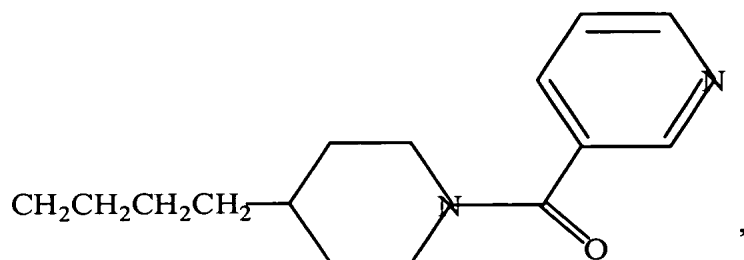
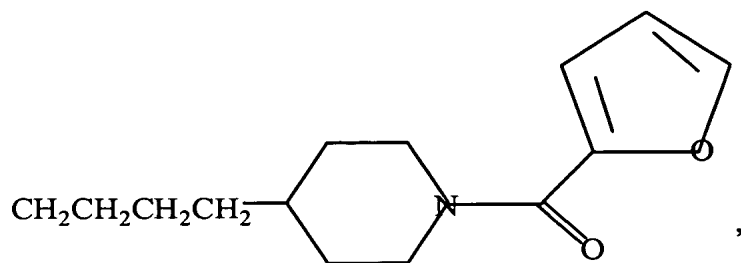


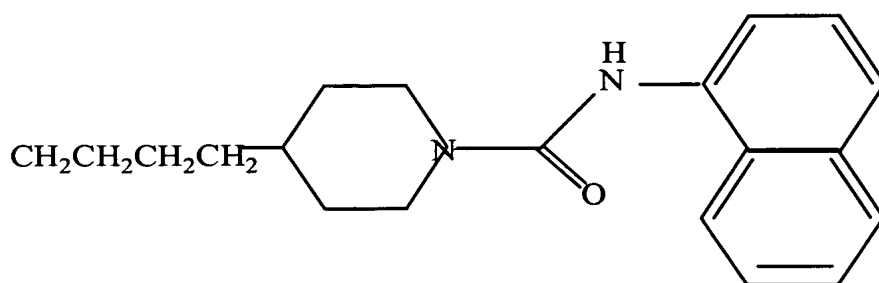
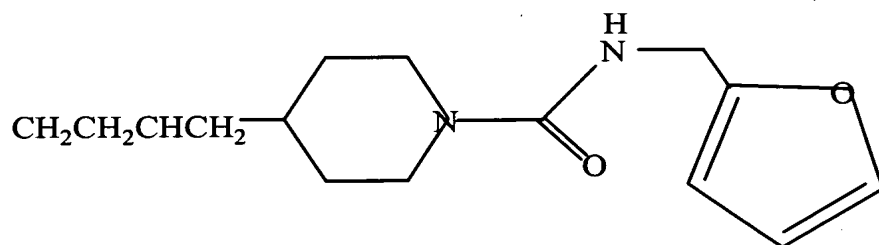
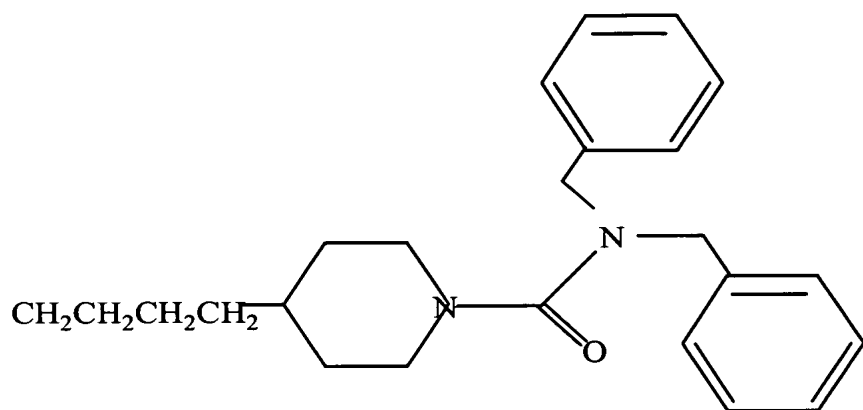
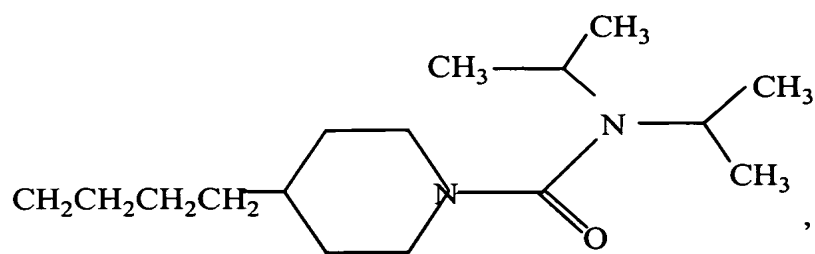


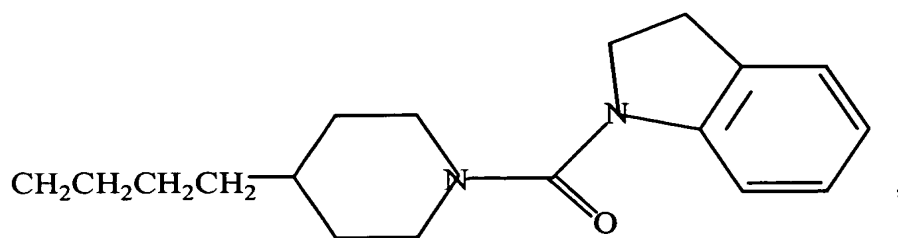
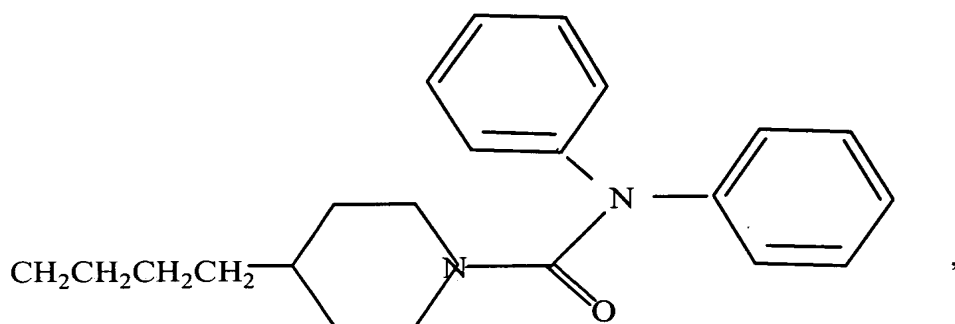
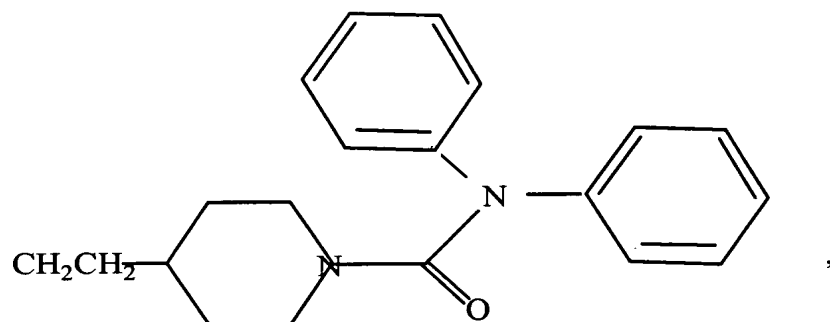
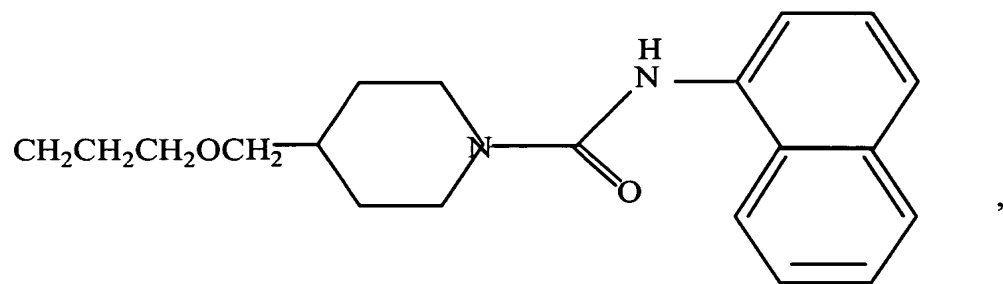


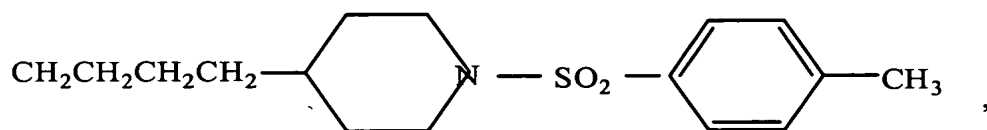
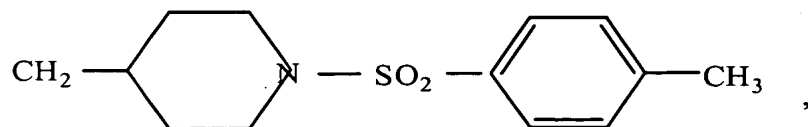
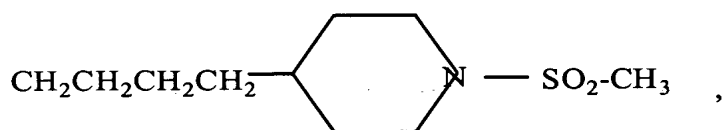
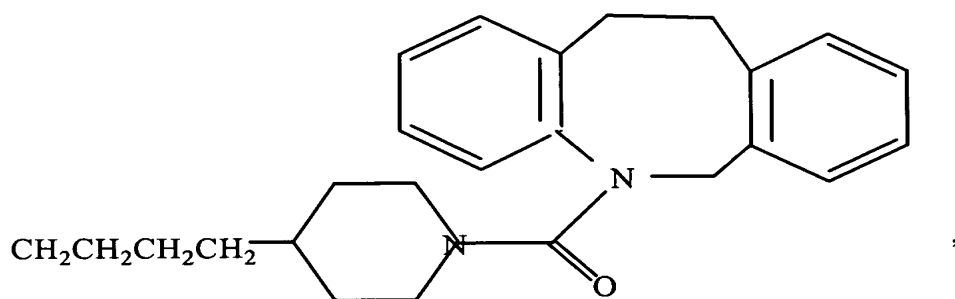
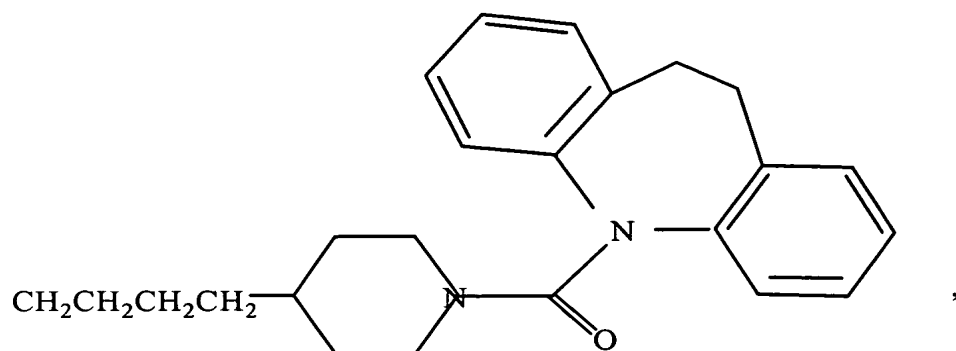


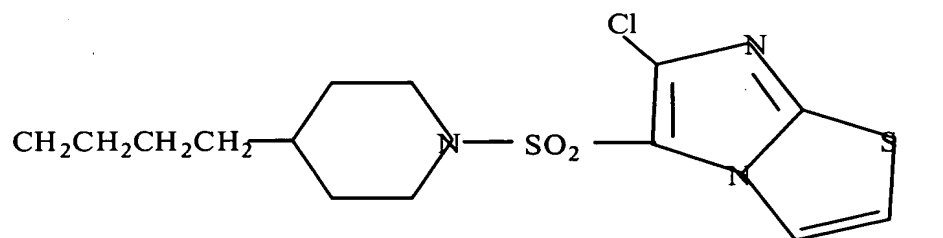
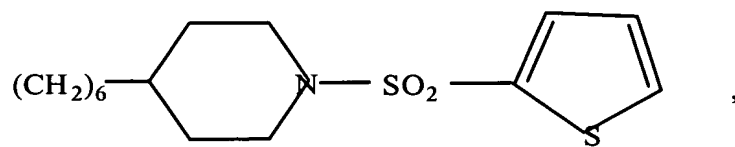
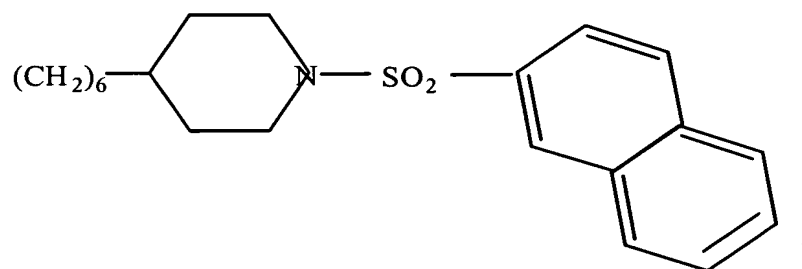
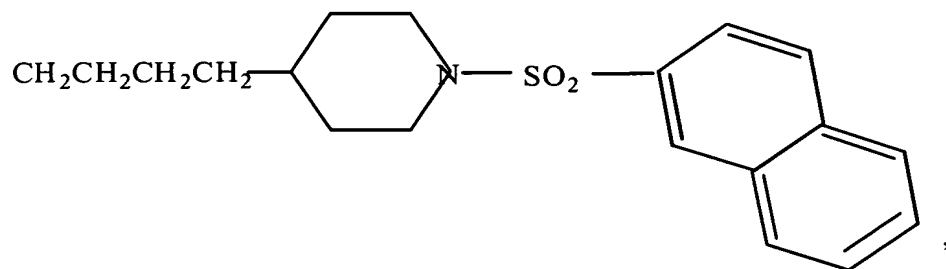
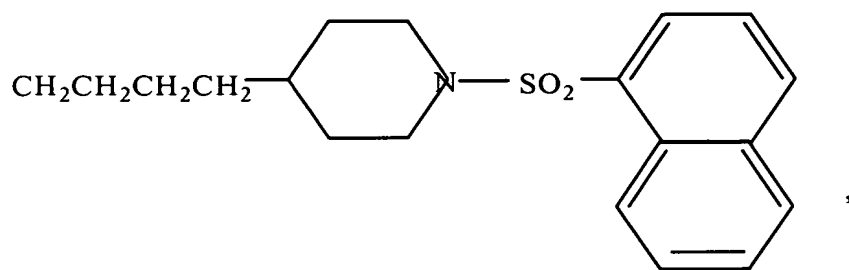


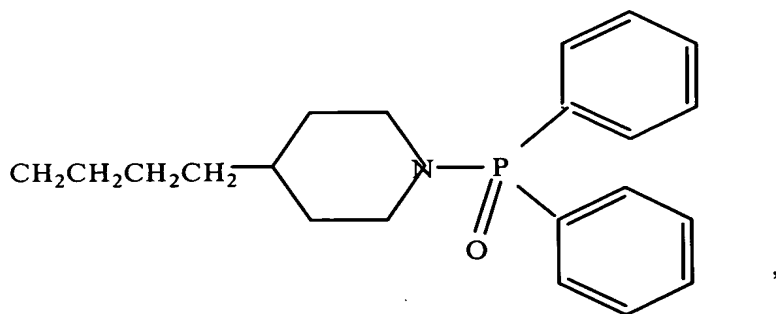
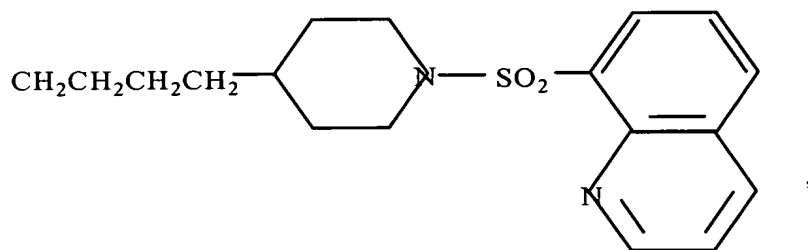
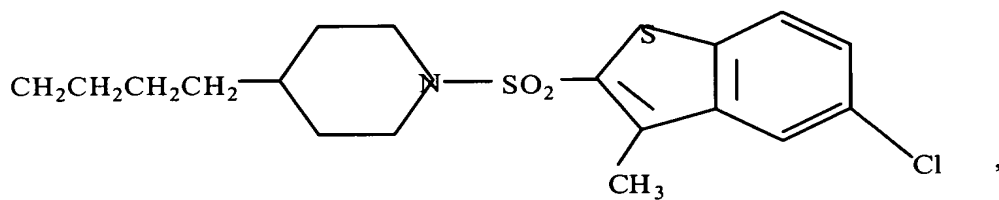
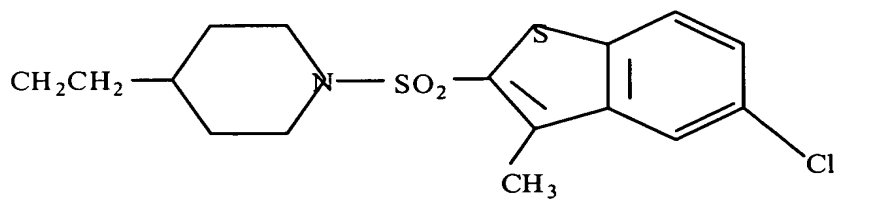
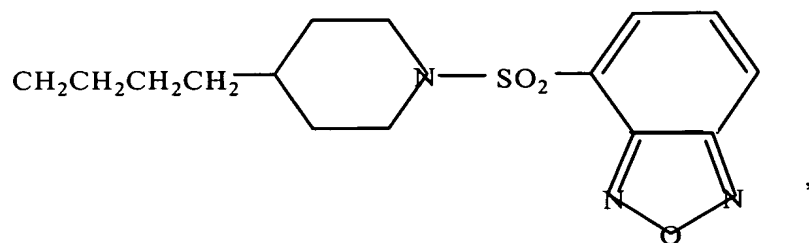


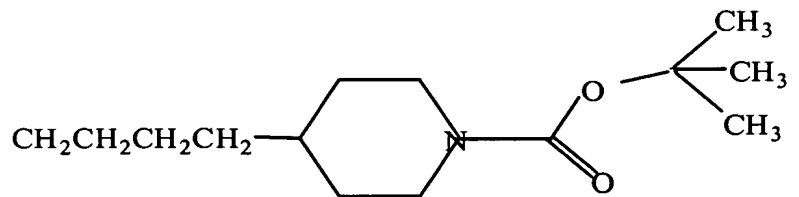
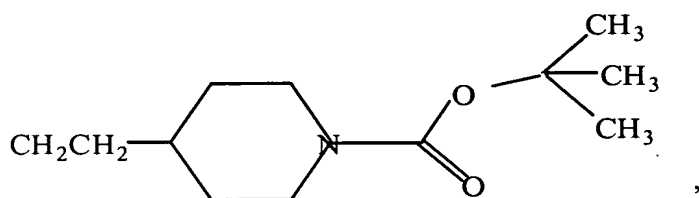
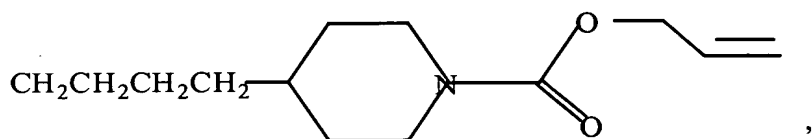
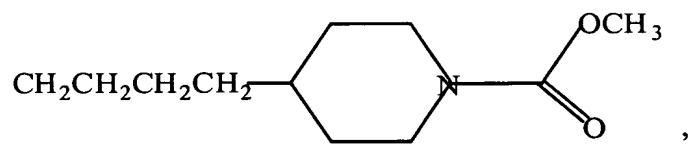
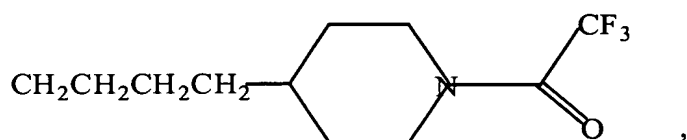
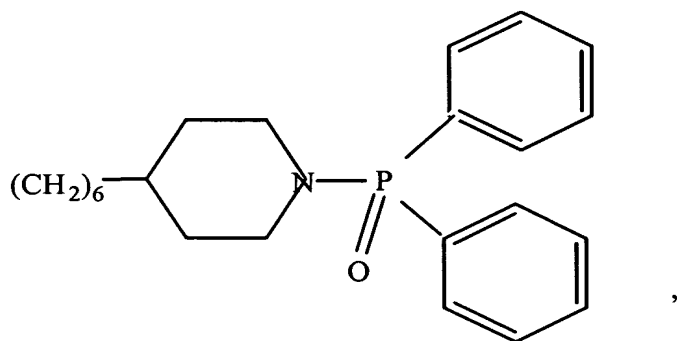


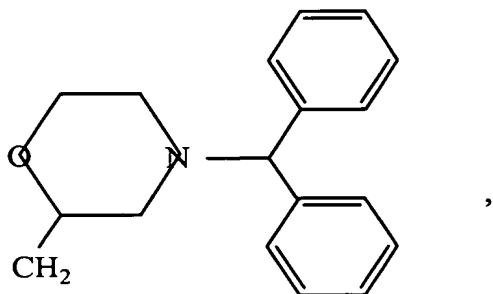
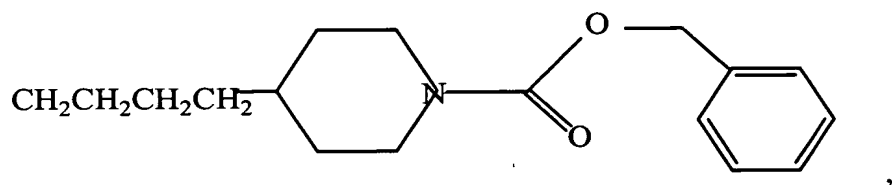
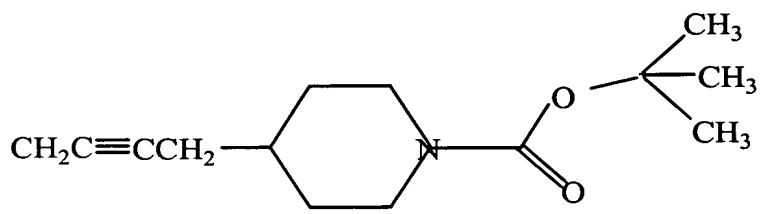
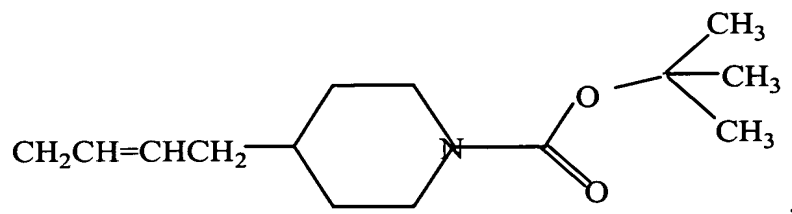
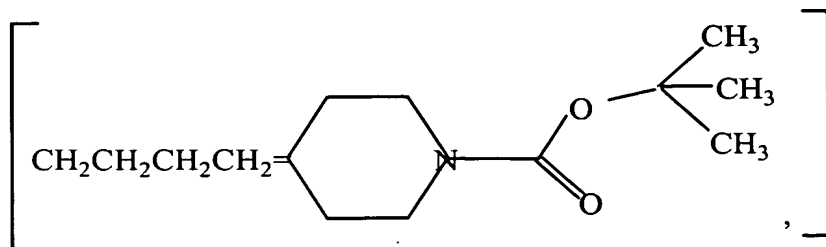


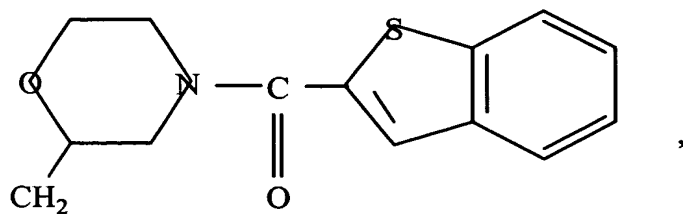
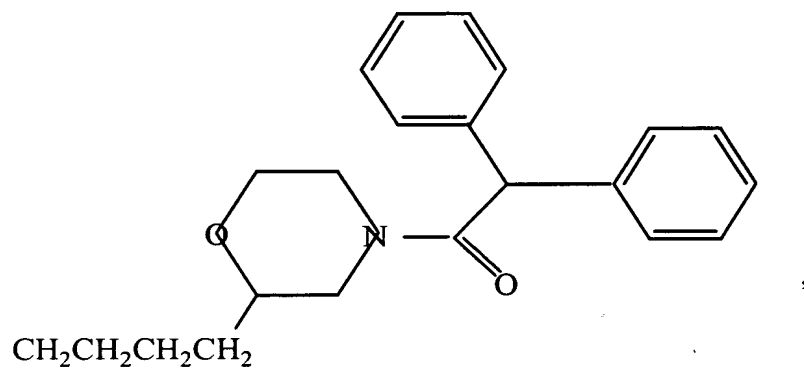
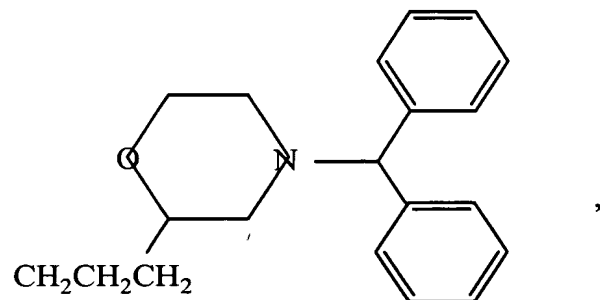
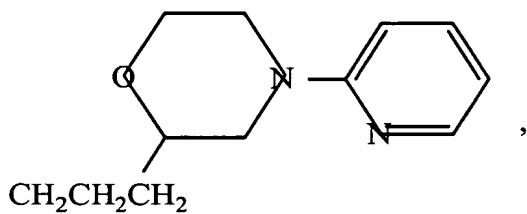


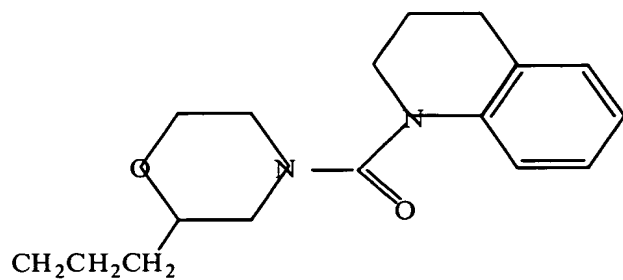




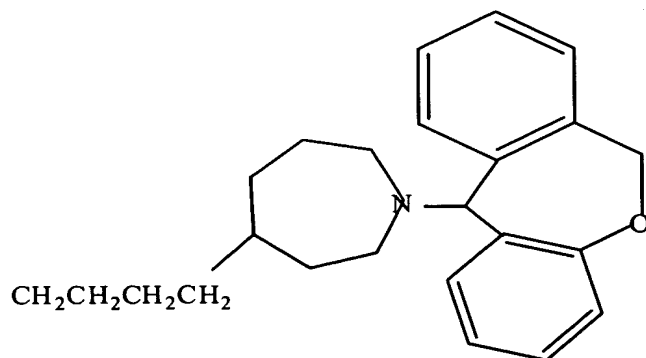
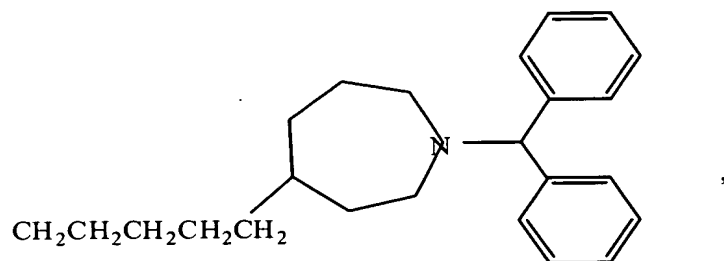
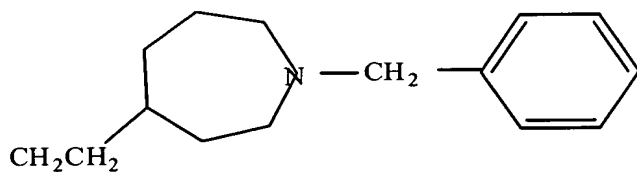
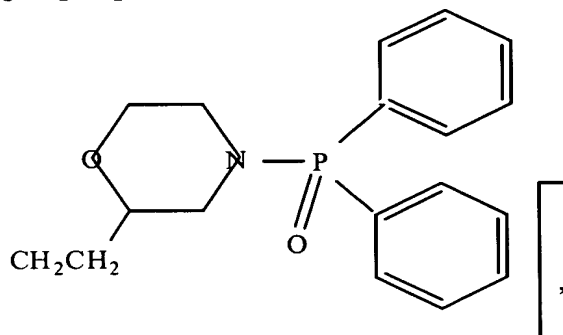


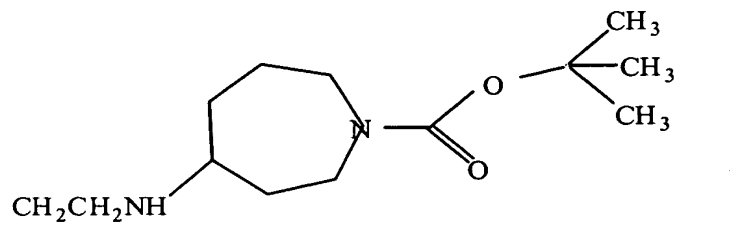
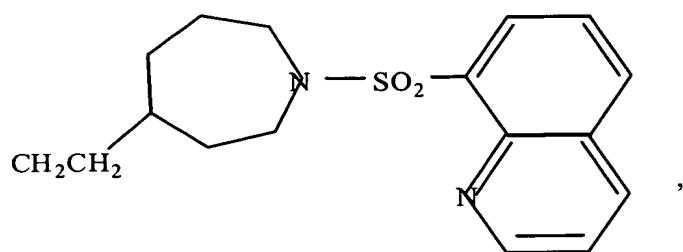
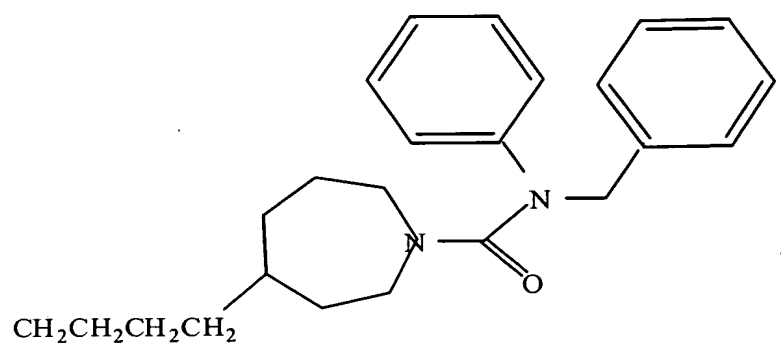
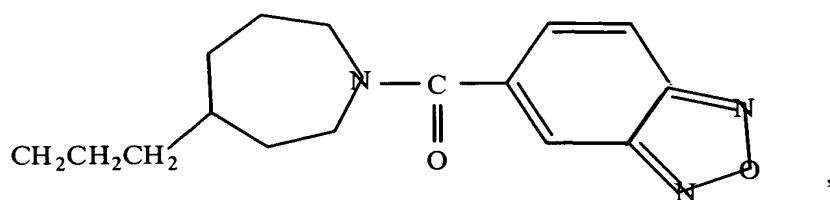
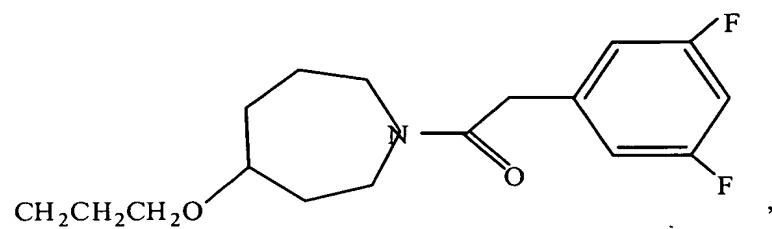


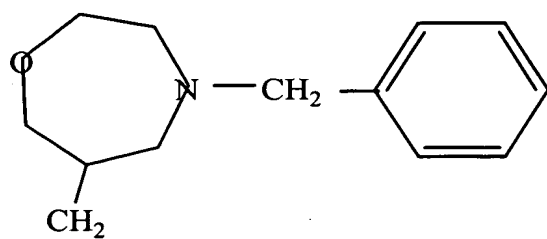
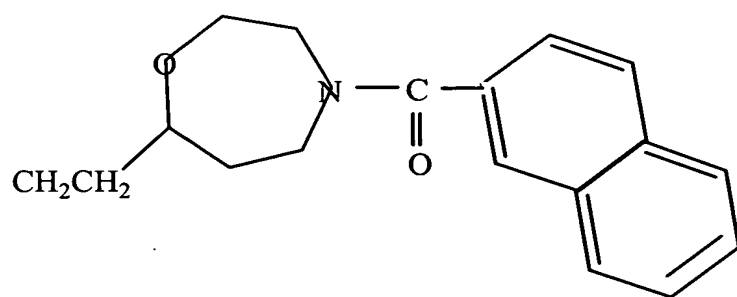
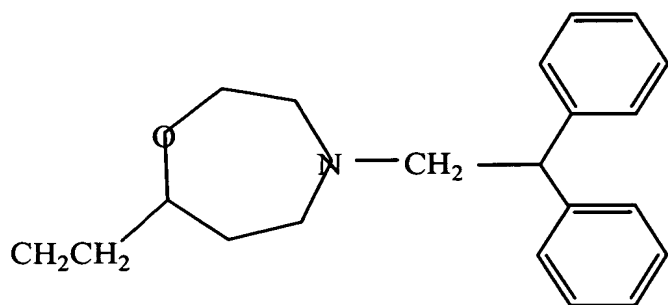




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